In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 8, 2024

DIANNE BYRD,	*	
Petitioner,	*	No. 20-1476V
v.	*	Special Master Gowen
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Andrew Downing, Downing, Allison & Jorgenson, Phoenix, AZ, for petitioner.
Jennifer A. Shah, United States Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

On October 27, 2020, Dianne Byrd ("petitioner"), filed a petition for compensation under the National Vaccine Injury Compensation Program.[2] Petition (ECF No. 1). Petitioner alleges that the Prevnar 13 vaccine she received on February 6, 2019 caused her to develop Guillain-Barre syndrome ("GBS"), "requiring extensive hospitalization and rehabilitation." *Id.* at Preamble. Based on a review of the evidence and testimony presented, I find that petitioner has established that she is entitled to compensation.[3]

I. Procedural History

[1] Because this Ruling contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Ruling will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to 34 (2012) (hereinafter "Vaccine Act" or "the Act"). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

[3] Pursuant to Section 13(a)(1), in order to reach my decision, I have considered the entire record, including all of the medical records, expert testimony, and literature submitted by the parties. This opinion discusses the elements of the record I found most relevant to the outcome.

Petitioner initiated her claim on October 27, 2020, alleging that the Prevnar 13 vaccine caused her to develop GBS. *Id.* To support her claim, petitioner filed extensive medical records from numerous facilities and affidavits by herself and her daughter. *See* Petitioner's Exhibit ("Pet'r Ex.") 1-9 (ECF No. 6, 9, 19).

Petitioner filed an expert report from neurologist Peter-Brian Andersson, M.D., Ph.D.[4] to address causation. *See* Pet'r Ex. 10 (ECF No. 22). The petitioner also presented the testimony of David Axelrod, M.D. as an expert in immunology.[5] *See* Pet'r Ex. 29 (ECF No. 45). The respondent filed an expert report from J. Lindsay Whitton, M.D., Ph.D,[6] and a Rule 5 conference was held on January 25, 2021. *See* Respondent's (Resp't) Ex. A (ECF No. 30). Supplemental expert reports were filed by both parties, with the government adding another expert, Peter Donofrio, M.D.[7] *See* Resp't Ex. C (ECF No. 32).

A two-day entitlement hearing was set after a second Rule 5 Status Conference and was held via Zoom on June 27 and 28, 2023. Both parties have filed post hearing briefs. *See* Resp't Post-Hr'g Br. (ECF No. 83); Pet'r Post-Hr'g Br. (ECF No. 84).

This matter is now ripe for adjudication.

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[4] Dr. Andersson is board certified in Clinical Neurophysiology and Neurology. He earned his medical degree from the University of Cape Town in South Africa in 1988 and earned his Doctor of Philosophy from the University of Oxford in the United Kingdom in 1991. He completed a neurology residency at the University of California, San Francisco in 1996. He went on to complete a neuromuscular fellowship at Oregon Health Sciences University and Stanford University. He worked as a clinical instructor at Stanford in 1999 and was a neurologist at Kaiser Permanente from 1999 until 2000. Dr. Andersson currently works as a Clinical Associate Professor of Neurology at the University of California, Los Angeles, where he has been since 2001. Throughout his career, Dr. Andersson has held a number of research positions for the National Research Institute. He also serves as the Medical Director for California Neurodiagnostics and California Alliance Neurodiagnostics. He is a member of the American Academy of Neurology, the American Association of Electrodiagnostic Medicine, and the American Medical Association.

[5] Dr. Axelrod is a graduate of the University of Michigan Medical School. After graduation he did fellowships in Internal Medicine and Allergy and Immunology at McGill University. He then did a research fellowship at NIH. He has had multiple teaching positions. He is board certified in Internal Medicine, Adult Rheumatology and Allergy and Immunology. He retired from clinical practice in 2018.

[6] Dr. Whitton is a board-certified immunologist and pathologist. He received his M.B., Ch.B, the equivalent of an M.D., from the University of Glasgow in Scotland in 1979. He earned his Ph.D. from the University of Glasgow in 1984. He is a member of the American Association of Pathologists, the American Association of Immunologists, the American Society of Virology, and the American Society of Microbiology. He has served on the editorial boards of numerous medical and scientific journals. He worked as a professor in the Immunology and Neuropharmacology at the Scripps Research Institute in La Jolla, CA from 1984 until 2017. He has authored or co-authored nearly 200 articles on an array of immunology topics.

[7] Dr. Peter Donofrio is a professor of neurology and Director of Neuromuscular Division at Vanderbilt University School of Medicine, and Director of the EMG lab at Vanderbilt University Medical Center. Resp't Ex. D. Dr. Donofrio received his medical degree from Ohio State University School of Medicine in 1975 and completed his internal medicine residency at Good Samaritan Hospital in Ohio. *Id.* Dr. Donofrio completed a neurology residency at the University of Michigan Medical Center and a neuromuscular fellowship at the University of Michigan. *Id.* He is board certified in internal medicine, neurology, electromyography and neuromuscular science. *Id.* Dr. Donofrio has experience in evaluating and caring for patients with neurological conditions, including transverse myelitis, Guillain-Barre syndrome ("GBS") and CIDP, among others. *Id.*

II. Evidence Submitted

a. Summary of Petitioner's Medical History

i. Pre-Vaccination

Petitioner retired from the University of New Mexico in May 2015, where she worked as a technical editor in the Technology Department for 28 years. Tr. 36. According to petitioner's and her daughter's testimony, petitioner was quite active in retirement working as an election official, taking classes at the University of New Mexico, attending world class performances at the local performance halls, travelling, and most significantly swimming a mile three times a week. Tr. 17, 36-37. She was planning to move to Texas to be near her daughter Brianne at the time of her vaccination. *See id.* at 45.

ii. Vaccination

Petitioner, 65 years old at the time, presented to her primary care physician for an annual exam on February 6, 2019. Pet'r Ex. 5 at 51 (ECF No. 6). Petitioner's chronic conditions included gastroesophageal reflux disease ("GERD") with a history of Schatzki's ring requiring dilation and recent EGD to remove stuck food, metabolic syndrome, history of smoking, obstructive sleep apnea ("OSA"), colon polyps, and osteopenia in the femoral neck. *Id.* at 53. She was also noted to have malignant essential hypertension controlled with Lisinopril. *Id.* at 51. On the date of her physical, her blood pressure was 126/78 with oxygen saturation of 97. *Id.* The social history notes that petitioner "retired in May [four] years ago, was a technical editor at the University of New Mexico Hospital, very active in her church. She does some occasional part time work. She is going to the gym a whole lot to swim." *Id.* at 52. Her noted habits included "is now swimming a mile at a time, which takes her an hour. She loves this. She eats a fairly healthy diet with excess sweets on top." *Id.* Petitioner was noted to live independently alone with four dogs and two turtles. *Id.* Petitioner received the pneumococcal 13-valent vaccine (Prevnar 13) in her left arm at this appointment. *Id.* at 54; Pet'r Ex. 4 at 3.

iii. February 13, 2019 Emergency Department Visit

Roughly four days post vaccination, petitioner began experiencing pain, numbness, and tingling in her feet and around her ankles that she described as "being like a deep ache." Tr. 48. This continued for several days, although she was able to go out and go shopping with a friend. *Id.* By February 13, 2019, the pain had gradually increased, and, by that evening, was up to her knees, prompting petitioner to call an ambulance to take her to the emergency room. *Id.* at 49.

Petitioner presented to the Emergency Department (ED) at Lovelace Women's Hospital on February 13, 2019 complaining of bilateral leg pain. Pet'r Ex. 6 at 5360. The history of present illness noted that petitioner had "[hypertension], plantar fasciitis, neuropathy unofficially diagnosed, and [obstructive sleep apnea]" and "present[ed] to ED via EMS [complaining of] gradual, constant, worsening, moderate-severe, non-traumatic bilateral feet pain on plantar and dorsal aspects described as sharp radiating to knees." *Id.* at 5364. Petitioner reported a gradual onset of the pain and that the pain was worsening. *Id.* The physical examination of the bilateral

ankles revealed "normal range of motion, no swelling, no deformity, [and] no tenderness." *Id.* at 5367. Physical examination of the bilateral lower legs showed "no tenderness, no bony tenderness, no swelling, no edema, no deformity, and no laceration." *Id.* The bilateral feet exhibited "normal range of motion, no tenderness, no bony tenderness, no swelling, normal capillary refill, no crepitus, no deformity, and no laceration." *Id.* The neurological exam revealed no sensory deficits, normal muscle tone, and normal coordination. *Id.* Petitioner's mood was noted to appear anxious. *Id.* An ultrasound was performed to check for deep vein thrombosis, which was negative. *Id.* at 5372, 5383-84. A progress note states, in part, that "the patient is feeling better and [is to] be discharged home. Patient's labs are all normal . . . Patient has no evidence of any injury to her legs. Patient seems to be having severe anxiety and is unable to tell why." *Id.* at 5363. Clinical impressions included anxiety and pain in both lower extremities. *Id.* Petitioner was given a valium prescription and discharged home. *Id.* at 5362.

iv. Admission to Lovelace Medical Center (February 16, 2019 – March 17, 2019)

Petitioner testified that over the next two days the pain continued to worsen and progressed all the way up her legs. Tr. at 51-52. Her neighbor did the grocery shopping for her. She was mostly laying on the bed. *Id.* Petitioner recalled that on the 16th, she attempted to stand, but fell. *Id.* at 52. Her neighbor brought a walker, which petitioner thought would help her stand. *Id.* However, when she tried to stand, her feet "just flopped down," she passed out, and her neighbor called an ambulance. *Id.* Petitioner presented to the Lovelace Medical Center Emergency Department via EMS on February 16, 2016 with complaints of worsening pain. Pet'r Ex. 6 at 16. EMS reported that petitioner's leg numbness started the previous night, and that she required maximum assistance to get to standing and to the gurney. *Id.* Petitioner reported that the numbness started at approximately 1900 the night before and that she fell about 10 times from the time of onset until she was at the ED. *Id.* The ED physician noted that petitioner's presentation was "unusual" with "bilateral leg pain occurring about [five] days lasting a day and a half, [and] now, true weakness of her quadricep muscles in both of her legs leading to frequent falls and bruising of both legs and arms." *Id.* at 8.

A review of systems was positive for weakness and numbness and for bilateral lower extremity pain. *Id.* A neurologic exam revealed abnormal gait and no Babinski's sign on either side. *Id.* at 12. Petitioner's reflex scores were: Tricep: 1+ on the right and 1+ on the left; Bicep: 1+ on the right and 1+ on the left; Brachioradialis: 1+ on the right and 1+ on the left; Patellar: 0 on the right and 0 on the left; Achilles 1+ on the right and 1+ on the left. *Id.* In the ER she had 4/5 strength in the bilateral quadriceps and 5/5 strength in the bilateral triceps, biceps, brachioradialis, hip flexors, ankle dorsiflexors, and ankle plantar flexors. *Id.* A CBC revealed an elevated white blood cell count at 17.0 (4.0 – 11.0). *Id.* at 21. The assessment included "generalized weakness with blurred vision – consider GBS per tele-neurology" and urinary tract infection ("UTI"). *Id.* at 8. Petitioner was admitted to the hospital. *Id.*

When petitioner arrived in her room, she reported to the nursing staff "new onset of blurred vision to her right peripheral vision with noticeable right arm and leg weakness." *Id.* at 54. A stroke alert was called, and petitioner underwent a head CT to rule out a stroke. *Id.* When she returned to the room, a neurologist evaluated her via tele-health. *Id.* at 34, 54. The

neurologist's summary states that petitioner came to the ED two days ago with "extreme pain in both legs," and significant bilateral lower extremity weakness for the past day. *Id.* at 34. It also notes that "in [the] ER, staff noticed diplopia, right face weakness, and some bilateral lower extremity weakness," with more weakness on the right than left. *Id.* On examination, her face had partial weakness, both arms had drift, both legs had some effort against gravity, and there was ataxia in two limbs. *Id.* The impression notes that the diplopia, weakness, and ataxia were "concerning for a variant of Guillain-Barre Syndrome versus CVA/cord lesions." *Id.* The neurologist recommended a lumbar puncture and brain MRI and noted that "if MRI [is] normal and [lumbar puncture] results show elevated protein, will need IVIG for possible Guillain-Barre Syndrome." *Id.* It was initially thought that she had a urinary tract infection and antibiotics were started. *Id.* at 23. However, the culture taken before starting antibiotics was negative and the antibiotics were stopped. *Id.* at 182.

An MRI of the thoracic and lumbar spine, performed on February 16, 2019, revealed "degenerative changes within the lumbar spine. . .without cord lesion or area of abnormal enhancement." *Id.* at 557. A head CT and brain MRI were done on February 17, 2019, and both were normal. *Id.* at 549, 552. Petitioner had multiple abnormal labs on February 16 and 17, 2019. On February 16, 2019, her CK level was significantly elevated at 3,092 (reference range 21-215), and her WBC was high at 17 (reference range 4-11). *Id.* at 669, 673. Labs taken on February 17, 2019, revealed a high Complement Total (CH 50) of 229 (reference range 60-144). *Id.* at 646. She had positive Mycoplasma IgG antibodies but negative IgM. *Id.* at 649. The lumbar puncture showed elevated CSF proteins of 72 (reference range 15-45) and slightly elevated CSF glucose of 71 (reference range 40-70). *Id.* at 651-52.

The hospitalist's history and physical taken upon petitioner's admission just after midnight on February 17, 2019 notes "5-day history of progressively worsening bilateral lower extremity weakness associated with tingling sensation and numbness which was seen last night. Patient also reported having recurrent falls as a result of lower extremity weakness." *Id.* at 17. Petitioner reported a gradual onset of her symptoms, and that she now could not walk without assistance. *Id.* She also reported "lower back pain, blurry vision, and poor urinary stream." *Id.* A neurologic examination revealed 4/5 strength of the bilateral quadriceps and 5/5 strength of the bilateral, triceps, biceps, brachioradialis, hip flexors, ankle dorsiflexors, and ankle plantar flexors. *Id.* at 20. Petitioner had an abnormal gait. *Id.* The diagnoses included "bilateral lower extremity weakness with numbness and blurry vision – etiology could be related to acute myelopathic radiculopathy versus Guillain Barre [versus] UTI." *Id.* at 23.

By the afternoon on February 17, 2019 petitioner reported feeling "weaker than she was last night and even weaker than she was this morning." *Id.* at 170. She was unable to raise her arms and felt numb in the arms and legs. *Id.* She had some blurry vision. *Id.* A neurologic examination revealed that petitioner had "almost no movement of all extremities" and had no grip strength. *Id.* at 171. Her sensory perception was significantly diminished in the arms, and she reported that her arms felt "as if she [had] been to the dentist." *Id.* The lower extremities had good dorsal and plantar flexion strength but had significantly decreased sensory perception. *Id.* Petitioner's neck strength was "relatively good" *Id.* Tele-neurology re-consulted and felt that petitioner had a variant of GBS. *Id.* at 36. They recommended a five-day course of IVIG and

transferring petitioner to the ICU for monitoring of petitioner's respiratory system, which was declining. *Id.*at 36, 173.

Petitioner was transferred to the Intensive Care Unit ("ICU") at 3:11 p.m. on February 17, 2019. *Id.* at 24. The ICU History and Physical states that petitioner "was seen in the emergency room a few days ago for bilateral leg pain and now she states that the pain has worsened. Patient's weakness has become worse with blurred vision. Patient admitted to ICU for possible airway compromise given weakness (possible GBS)." *Id.* By this time, petitioner displayed abnormal reflex and coordination on her neurologic examination, and her motor strength was 2/5 in the bilateral legs and arms. *Id.* at 27.

The following day, on February 18, 2019, petitioner's bilateral upper and lower extremity weakness appeared slightly worse. *Id.* at 174. A neurologic examination revealed 2/5 strength in the bilateral upper and lower extremities. *Id.* at 176. Petitioner reported to nursing staff that she felt like she could not breathe. *Id.* at 69. Later in the day, petitioner was placed on a feeding tube, as speech pathology determined that she had a high risk of aspiration "due to progressive weakness." *Id.* at 29.

On February 19, 2019, petitioner was noted "to be very weak and unable to complete full sentences with taking a breath." *Id.* at 356. Respiratory Therapy intubated and sedated petitioner at 12:58 on February 19, 2019 "due to resp[iratory] fatigue and deterioration in respiratory mechanics due to presumed GBS." *Id.* Another neurology consultation occurred after petitioner's intubation. *Id.* at 39. The History of Present Illness notes that petitioner "was still using her arms and hands on Sunday 17-Feb, though her hands were 'floppy' and her leg weakness was greater than her hands which was greater than her arms." *Id.* Petitioner's daughter reported "seeing some [right] facial droop, particularly with the eyelid." *Id.* The daughter also reported that petitioner had "continued to weaken and was intubated earlier" in the day "to assist her breathing efforts." *Id.* Petitioner was noted to be "speaking with diminishing effort prior to intubation." *Id.* During the physical examination, petitioner would communicate through nodding or mouthing. *Id.* at 43. Her mental state was "in and out of arousal with intubation sedative." *Id.* Examination of the cranial nerves was significant for diplopia and slowed gaze "in all directions more so horizontally to [left/right] than up/down," and prominent ptosis of the right eye with the eyelid fatiguing quickly upon upward gaze. *Id.* The sensory exam was noted to be difficult to test in petitioner's awake/intubated state, but sensation appeared to be "markedly diminished in the bilateral lower extremities to touch, vibration, and temperature." *Id.* Petitioner was areflexic and demonstrated "generalized weakness of [the] entire body" with the bilateral lower extremities worse than the bilateral upper extremities. *Id.* By February 20, 2019, her strength was rated 0/5 in the bilateral arms and 1/5 in the bilateral legs. *Id.* at 38.

Neurology followed up with petitioner on February 25, 2019, and noted that petitioner had "onset of burning and tingling and numbness of the feet progressing over a day to some weakness. The symptoms were symmetrical, distal worse than proximal. The weakness rapidly became severe, unable to walk." *Id.* at 241. On examination, petitioner had 2/5 strength in the bilateral arms and legs and areflexia in all limbs. *Id.* at 242. The assessment noted that petitioner's presentation was "most consistent with severe GBS the axonal motor subtype

clinically. Severe respiratory weakness required intubation. Steady improvement after 5 days of IVIG." *Id.*

On February 26, 2019, the critical care physician noted that petitioner's exam had "definitely worsened" compared to the day before. *Id.* at 243. On examination, petitioner looked "significantly more distressed when compared to yesterday. On exam, her eyelids show lid lag when compared to yesterday. More on the right side. Decreased gag. Her strength in upper extremity is much decreased. Unable to clench my fingers. Lower extremities still have strength against resistance." *Id.* at 245.

Petitioner was extubated on March 1, 2019, but required re-intubation on March 5, 2019 due to respiratory distress and hypoxia. *Id.* at 167, 245, 290. She developed respiratory alkalosis and liver dysfunction *Id.* at 290, 305. After failing multiple weaning trials, petitioner underwent a tracheostomy on March 8, 2019. *Id.* at 169. On March 4, 2019, petitioner was noted to be alert, weak appearing, able to move lower and upper extremities, however still extremely weak with right ptosis." *Id.* at 274. Throughout this admission, petitioner had labile blood pressure which was occasionally uncontrolled and thought to be "due to autonomic dysreflexia associated with GBS." *Id.* at 190. Her strength fluctuated throughout her admission, but she remained "very weak and only able to minimally move [her] extremities." *Id.* at 284. She complained of leg pain throughout the admission as well. *Id.* at 294, 308.

Petitioner was discharged to Covenant Health, a long-term care facility, on March 17, 2019. The discharge summary notes that throughout petitioners' month-long admission, she "developed several hospital-acquired infections including pseudomonal pneumonia." *Id.* at 438. The discharge summary further summarized her course, noting that "7-10 days prior had her flu [sic] shot and then [five] days prior to admission developed progressive bilateral extremity weakness with tingling and numbness." *Id.* She was then "transferred to the ICU…and intubated shortly thereafter." *Id.* She underwent several extubations, eventually leading to her having a PEG tube and trach placed. *Id.* Upon her discharge, "she was making progress with her trach mask trials tolerating 8-10 hours in the day and returning on the vent at night." *Id.* Her discharge diagnoses included, in part, bilateral leg weakness, GBS (Guillain Barre syndrome), leukocytosis, OSA (obstructive sleep apnea), acute respiratory failure with hypoxia, and generalized weakness. *Id.* at 436.

v. Long Term Care Facilities

In the two years and nine months following petitioner's discharge from Lovelace Medical Center on March 17, 2019, she was admitted to four different long term care facilities. She was admitted to Covenant Health from March 17, 2019, until April 26, 2019, after which she was transferred to Trustpoint Rehabilitation Hospital. She remained at Trustpoint from April 26, 2019, until May 27, 2019. Petitioner was re-admitted to Covenant Health from May 27, 2019, until June 27, 2019. Following this admission, she was a patient at South Plains Rehabilitation Hospital until August 12, 2019. She was transferred to Lakeside Nursing home on August 12, 2019, where she resided until she was discharged to her daughter's home in December of 2021.

At Lakeside, petitioner's chart noted acute and chronic respiratory failure, GBS, neuromuscular bladder dysfunction, functional quadriplegia, muscle weakness and wasting, and major depressive disorder. Pet'r Ex. 9 at 6.

Petitioner was later admitted to a rehabilitation hospital affiliated with Texas Tech University Health Science Center in December 2022 where her intensive rehabilitation efforts were supervised by Dr. Farooq, who testified that despite intensive efforts petitioner did not improve significantly. Tr. 163. She remained in-patient at this facility for four weeks in December 2022 and January 2023. Petitioner said that when she came home from that rehabilitation, she was able to raise her right hand more to where she can almost brush her hair. Tr. 60. Petitioner is able to brush her teeth. *Id.* Petitioner said that "there are things happening like that that she considers progression." Tr. 58.

b. Testimony and Affidavits

i. Brianne Mireles

Petitioner's daughter, Brianne Mireles, testified at the hearing. She has a master's degree in nursing education and her national board certification in geriatric and palliative care. *Id.* at 15. At the time of the hearing, she worked as a charge nurse at the University Medical Center (UMC) in Lubbock, Texas on an orthopedic trauma floor. *Id.* at 14. The UMC is a Level I Trauma Center. *Id.* She previously worked as a registered nurse on a renal medical-surgical floor and on the palliative and geriatric care floor. *Id.* at 15.

Ms. Mireles testified to her mother's life prior to the onset of her Guillain-Barre Syndrome, stating that petitioner "was living her best life. She was retired, so she could do what she wanted, when she wanted it." Tr. 16. She testified to some of the activities petitioner enjoyed prior to receiving the vaccine, including volunteering with the food distribution program at her church, volunteering with voting services during elections in New Mexico, and swimming "miles a week." *Id.*at 16-17. Petitioner travelled from Albuquerque, New Mexico to visit Ms. Mireles in Lubbock, Texas and to visit friends in Arizona. *Id.* at 17. In the months prior to her vaccination, petitioner traveled with her daughter and son in law to Juneau, Alaska and participated in a salmon deep sea fishing tournament. *Id.* Ms. Mireles testified that there were no "restrictions on what [petitioner] was able to do." *Id.*

Ms. Mireles testified that petitioner first mentioned complaints following the vaccine during a phone call on February 10, 2019. Tr. 19. Petitioner complained of some pain and numbness in both of her legs but was still able to walk and was generally herself at this point. *Id.* Ms. Mireles next spoke to petitioner on February 13, 2019, when petitioner was discharged from the emergency department. Petitioner stated she was just having a little more severity with the same symptoms. *Id.* at 19- 20. On February 16, 2019, Ms. Mireles checked the petitioner's location on her phone, and noticed that petitioner was back at the hospital. *Id.* Ms. Mireles arrived the next day, on February 17, 2019, and participated in the care of her mother. *Id.*

Ms. Mireles recalled that, throughout petitioner's admission to Lovelace, petitioner could not move her legs or her arms at all. Tr. at 25. She could "barely hold her eyes open," which they

taped open at one point. *Id.* at 26. Petitioner was transferred by ambulance to a long-term facility in Lubbock, Texas to be near where Ms. Mireles lived. *Id.* It was about six months before Ms. Mireles saw any improvement in petitioner's motor movement, but the improvement was not "really in the extremities" at that point. *Id.* It wasn't until she was at Trustpoint Rehabilitation that they saw improvement with petitioner able to "use a soft touch call light," which allowed petitioner to call for help by moving her hand to tap the pad. *Id*. Petitioner also developed various respiratory and urinary tract infections. *Id.* at 28.

Petitioner eventually moved into her daughter's home. Tr. 31. Over the last four years there has had very little improvement. *Id.* at 28. Petitioner is unable to stand on her own, walk, shower, go to the bathroom by herself, or do anything she did before. *Id.* at 29. Ms. Mireles had a Hoyer lift installed to help transfer petitioner out of bed. *Id.* at 30–31. In the eight months leading up to the hearing, petitioner got AFOs, which are custom braces for her legs which allows them to not use the Hoyer lift as much. *Id.* According to Ms. Mireles, the biggest improvement in the year leading up to the hearing is that petitioner does not require use of the Hoyer lift to get out of bed as often, but there are still times when it is necessary. *Id.* at 33-34. At the time of the hearing, petitioner was able to sit in a wheelchair, but her improvement has been minimal. *Id.*

At the time of the hearing, petitioner participated in rehabilitation only intermittently, as she must get insurance re-authorization. Tr. 33. However, petitioner has plateaued, making re-authorization difficult to obtain due to a lack of significant improvement. *Id.* Petitioner has gone through her savings and her daughter's family savings to cover medical costs. *Id.*

ii. Dianne Byrd

Petitioner testified at the hearing from her daughter's home and testified consistently with the medical summary provided above regarding the onset of her GBS and to the facts of her paralysis throughout her first hospitalization. *Id.* at 34-67. She testified about her prior activities, in particular about swimming a mile at a time three days a week which she had done for about two years at the time of the onset of her GBS. *Id.* at 38. She testified that she was planning to move out of state to be near Brianne, so she scheduled a final physical with her long-time physician, Dr. Lemmon on February 6, 2019, during which she received the Prevnar 13 vaccine. *Id.* at 45, 47. She briefly described the early symptoms and hospitalization. *Id.* at 49-56.

Focusing on the present time, petitioner testified that she needs help 24 hours a day, seven days a week. Tr. 57. However, because she cannot afford around the clock care, she and her daughter have a "minimum schedule of what can work in order to take a lot of the load off" petitioner's daughter. *Id.* This schedule involves caregivers coming three hours in the morning and three hours in the late afternoon seven days a week, which costs about $1,000 per week. *Id.* She is unable to get out of bed to a standing position without the aid of a caregiver, even with the AFOs, and she wears diapers. *Id.* at 58. Most of her physical therapy focused on her lower body, but she also had some occupational therapy in 2022 to help with her arm and hand strength and dexterity. *Id.* Petitioner is now able to hold her phone and text and she can hold a cup, though "very awkwardly." *Id.* at 58-59. She described these as significant milestones that have given her some additional quality of life. *Id.* In January 2023, petitioner spent four weeks in a rehabilitation

hospital, after which she was able to raise her right hand more to where she can almost brush her own hair. *Id.* at 60. She is able to brush her teeth. *Id.* at 59.

Petitioner testified about the financial hardship she has faced as a result of her GBS. At the time of the hearing, petitioner had gone through her savings and relies on credit cards to pay for the caregiving. Tr. at 60-61. She has maxed out one card with the largest credit limit and was close to maxing out a second which she uses for caregiving. *Id.* at 61. She has relied on her family to pay for some of her medical treatment, including her brother who paid $5,000 for the ambulance to transfer petitioner from Albuquerque to Lubbock. *Id.* Petitioner also explained that the pressure on her daughter has been heavy with her working a full-time job then coming home to take over petitioner's care. *Id.* at 62-63. This has also led to an adjustment in petitioner's relationship with her daughter, where Ms. Mireles is now her caregiver, and she is helpless. *Id.*

iii. Dr. Asir Farooq, M.D.

Doctor Asir Farooq testified as one of Ms. Byrd's treating physicians. *See* Tr. 157-66. He explained that he is a hospital-based internist and has been for fifteen years. *Id.* at 158. He is board certified in internal medicine. *Id.* at 159. He is employed at Texas Tech University Health Science Center, which is a 500 bed, level one trauma center serving a population of over one million people in West Texas and Eastern New Mexico. *Id.* at 158. They receive many referrals from community hospitals and handle a lot of complex patients. *Id.*

Dr. Farooq treated Ms. Byrd, beginning in December 2022, in the rehabilitation hospital. Tr. 161. He was not involved in her original hospitalization. *Id.* He took a detailed history when he met her and understood that prior to February 2019, she was very functional and independent and did not have any neurological deficits. *Id.* at 162. He understood that everything else was ruled out and that it was thought that the vaccine could have contributed to her GBS. *Id.* They did aggressive therapy in the rehab facility, but she did not improve significantly. *Id.* at 162-63. Based on the history, ruling out alternative causes, and the timing of her disease, Dr. Farooq opined that it was likely that the Prevnar vaccine caused petitioner's GBS. *Id.* at 163.

c. Expert Witness Opinions on Causation

i. Petitioner's Experts

1. Dr. Peter-Brian Andersson, M.D., PhD.

Dr. Andersson was admitted as an expert in neurology and neuroimmunology. Tr. 78. His credentials are described above. His CV was filed as summarized above. In short, Dr. Andersson is board certified in neurology, is actively engaged in the practice of neurology, and has had a long-standing interest in neuroimmunology. *Id.* at 74, 77. He has treated between 150 and 250 patients with GBS in his career. *Id.* at 75. Dr. Andersson filed an initial report as well as a rebuttal report in this case. *See* Pet'r Ex. 10; Pet'r Ex. 28 (ECF No. 37).

Dr. Andersson testified that he reviewed petitioner's medical history. Tr. 78. From a neuromuscular standpoint, she was normal prior to February 6, 2019. *Id.* He noted that she was

swimming regularly a mile at a time. *Id.* In reviewing the note of her annual physical on February 6, Dr. Andersson saw no indication of the development of GBS. *Id.* at 79. He generally described the peripheral nervous system, explaining that it is part of the nervous system that travels to and from the spinal cord sending and transmitting signals from the brain to the rest of the body as well as receiving and transmitting signals from the body to the brain. *Id.* at 80-81. He further described how signals are transmitted over axons that can be as long as a meter. *Id.* at 82. The axons are insulated by myelin which is wrapped around them and enables rapid transmission of signals. *Id.* He described saltatory conduction by which electrical signals are conducted over myelinated axons to points where there are gaps in the myelin known as the nodes of Ranvier. *Id.* When the myelin is damaged, the charge that is conducted over the axon can be lost, and with significant loss of myelin the slowed or lost signal can cause a loss of function. *Id.* at 82-83.

Dr. Andersson testified that GBS gives rise to a collection of symptoms and signs which constitute a syndrome of an autoimmune attack on the peripheral nervous system, "which produces a variable constellation of motor, sensory and autonomic symptoms and signs that are associated histopathologically" with an autoimmune attack. Tr. 83. Dr. Andersson explained that GBS occurs when the host immune system launches a humeral and/or cell mediated attack on the peripheral nerves. *Id.* at 84. Sometimes patients have a good recovery and other times not, but generally the more severe the initial attack, the worse the outcome. *Id.* at 83.

Dr. Andersson testified that this autoimmune attack on the nerves has been demonstrated in animal models generating a condition known as EAN, Experimental Autoimmune Neuritis. Tr. 84. EAN has been produced by the injection of nerve cells or specific immune cells, such as T-cells, "that react to specific proteins in the nerve and is associated with the histopathology of immune mediated injury" to the nerve. *Id.* Dr. Andersson also noted that GBS can be triggered by an activation of the immune system. *Id.* at 85. It is associated with an infection about 60% of the time and is also associated with vaccinations and surgery. *Id.* In general, GBS "is considered to be the result of an aberrant or self-directed immune attack produced by some trigger of the immune system," typically by infection. *Id.* at 85-86. He illustrated his testimony with reference to a chart from Goodfellow demonstrating the appearance of a nerve and the myelin wrapping of the axon. *Id.* at 86; Pet'r Ex. 12 at 6. [8] The chart illustrates the proposed mechanism of GBS pathogenesis by the immune response to the bacteria *Campylobacter jejuni*.[9] Tr. 86; Pet'r Ex. 12 at 6. The illustration was described in the article as showing;

[8] John Goodfellow & Hugh Wilson, *Guillain Barre syndrome: a century of progress*, 12 Nature Reviews Neurology 723 (2016).

[9] *Campylobacter jejuni* is a gram-negative bacterium, a leading cause of gastroenteritis and is the most common antecedent microorganism in GBS. A prospective case-controlled study detected evidence of recent *C. jejuni* infection in 26% of GBS patients. Nortina Shahrizaila & Nobuhiro Yuki, *Guillain Barre Syndrome Animal Model: The First Proof of Molecular Mimicry in Human Autoimmune Disorder*, Journal of Biomedicine and Biotechnology, Dec. 2010, at 2.

> A molecular mimic of gangliosides[10] present on peripheral nerve membranes from the lipooligosaccharides in *C. jejuni* which bind to the gangliosides at the node of Ranvier. Consequent activation of complement leads to the disruption of voltage-gated sodium channel clusters, disruption of the nodal architecture, and formation of the membrane attack complex, which leads to calcium influx. These changes cause axonal injury and attract macrophages, which can then migrate between the axon and myelin.

Pet'r Ex. 12 at 6. Dr. Andersson went on to explain that when the immune system recognizes a foreign invader, such as a bacterium like *C. jejuni*, which typically enters through the gut, "the infection is cleared by antigen presenting cells, which generate a T and B-cell mediated response." Tr. 87. Again, pointing to the Goodfellow diagram, he explained that the B-cells are stimulated by the infection. *Id.*; Pet'r Ex. 12 at 6. The B-cells mature to plasma cells which produce up to 2,000 antibodies per second and are then directed at the epitopes that were presented to the B-cells. Tr. 87-88. He further explained that "the antibodies are destructive by opsonizing" or making the invader cell look attractive "for further phagocytosing macrophages, which are cells that will basically gobble up that area and deposit a protein called complement which are destructive of the invader and will also trigger some degree of cell-mediated immune response or cell cytotoxicity." *Id.* The point being that the antibodies that circulate against the bacteria also circulate through the body and at times will bind to the host tissue such as a ganglioside on the axon, generating the same kind of toxic attack from what become anti-ganglioside antibodies and are now binding to the host axon. *Id.* at 88-89. This causes complement deposition "which generates a membrane attack complex, which is essentially punching a hole in the axon" allowing calcium to come into the cell. *Id.* This response also generates "chemoattractants and invasion of the tissues by macrophages" which phagocytose, or eat the tissue, and "also generate chemical mediators which amplify the immune response." *Id.* In short, Dr. Andersson said that this process described in the Goodfellow paper demonstrated how what starts as an immune response to the invading bacteria, ends up being an attack on the host tissue. *Id.* at 89.

Dr. Andersson testified that multiple articles lay a foundation for the concept of molecular mimicry, which occurs when there is sufficient similarity between the structure of the foreign invader and a structure of the host such as myelin. Tr. 90-92; *see e.g.,* Pet'r Ex. 19 at 2. The immune system is stimulated to attack an invader such as a viral or bacterial infection but can also cross react and attack the host peptides that look similar to those found in the invader. Tr. 90-92. He testified that vaccines can also produce a similar immunological process. *Id.* at 92. He said that when there is "an immune response generated to an infection, there is immune activation." *Id.* at 92-93. Similarly, "vaccination is an attempt at activating the immune system to produce a response to the inoculant." *Id.* at 93. When the immune system attacks the vaccine antigens, it may also recognize host antigens and cross react. *Id.* So, both infections and vaccines engage the immune system, and both can cross react. *Id.*

[10] "Gangliosides constitute a large family of predominantly cell-surface glycosphingolipids bearing a ceramide moiety anchor in the external leaflet of the lipid bilayer and a sialylated oligosaccharide core exposed in the extracellular space." *Id.*

Dr. Andersson was asked whether, based on the models described in his testimony and in the literature, the pneumonia vaccine can be an immunological trigger for GBS. Tr. 107. He testified that, just as an infection would trigger an immune response, the captured antigens in the vaccine trigger a cellular and humeral immune response with cooperation from the innate immune system. *Id.* To the extent that there are similar epitopes present on host peripheral nerve system tissue, the vaccine, in triggering an immune response, can now trigger the immune cells to attack the host through the effector mechanisms which then produce injury to the peripheral nerves. *Id.* at 107-108. The attack on the peripheral nerves then "produces the weakness, numbness, pain, and autonomic abnormalities." *Id.* at 108.

Dr. Andersson referenced a case report by El Khatib, which described a 13-year-old patient who presented with severe symptoms of streptococcus pneumonia and went on to develop GBS. Tr. 93-95; Pet'r Ex. 17 at 2-4. [11] El Khatib noted that mycoplasma pneumonia and influenza like illnesses and non-infectious causes like vaccination and surgery have been considered triggering factors in pediatric GBS. *Id.* He theorized that the "triggering factor evokes [an] immune response that cross reacts with peripheral nerve components because of the sharing of cross-reactive epitopes (molecular mimicry) [and] this immune response is directed toward the myelin or axon of the peripheral nerve." *See* Pet'r Ex. 17 at 3. El Khatib suggested that "pneumococcus has antigens which triggered an immune response and cross-reacted with peripheral nervous system surface components" in his patient by molecular mimicry, "due to the natural transformation of the streptococcus pneumonia's capsular polysaccharide." *Id.* This article also referenced two case reports of older people who developed GBS post streptococcus pneumonia infections. *Id.*

Dr. Andersson also referenced a case report by Bianchi which presented the case of a 78-year-old man who developed GBS four days after admission to the hospital with pneumococcus pneumonia. Tr. 95-98; Pet'r Ex. 18.[12] The GBS was characterized as mixed acute motor axonal and acute inflammatory demyelinating with prolonged cardiovascular features requiring mechanical ventilation. Pet'r Ex. 18 at 2. Bianchi theorized that "autoantibodies directed against peripheral nerve antigens, particularly gangliosides have been identified in patients with" GBS. *Id.* He indicated that "this case may explain why different infections associated with GBS may contribute to the clinical and immunological variety of this disease." Tr. 97-98; Pet'r Ex. 18 at 2.

Finally, Dr. Andersson discussed the article by Haber which is frequently cited in cases involving the association between the Prevnar vaccine and GBS. Tr. 98-106; Pet'r Ex. 21 at 4-5.[13] In this paper the authors looked at cases of GBS following vaccination with the Prevnar vaccine as reported to VAERS between 2012 and 2015 and found eleven such cases. Tr. 98-99; Pet'r Ex. 21 at 4. They discounted three of the cases as not meeting the Brighton diagnostic

[11] Hassan El Khatib et al., *Case Report: Guillain-Barre syndrome with pneumococcus – A new association in pediatrics*, 11 ID Cases 36 (2018).

[12] Giorgia Bianchi & Guido Domenighetti, *Pneumococcus pneumoniae infection and Guillain-Barre syndrome: fortuitous or specific association?*, 32 Intensive Care Med 338 (2006).

[13] Penina Haber et al., *Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 19 years old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012 – December 31, 2015*, 34 Vaccine 6330 (2016).

criteria for GBS, although they had physician diagnoses. Tr. 139. The reported cases occurred within two to thirty-four days post vaccination, which Dr. Andersson indicated was consistent with his experience in terms of time to onset. *Id.* at 100; Pet'r Ex. 21 at 4. Dr. Andersson testified that Haber identified multiple cases of GBS following Prevnar vaccination. Tr. 104; Pet'r Ex. 21 at 5. The authors concluded that GBS following Prevnar vaccination amounted to 0.7 cases of GBS per million and concluded that this did not represent a safety signal. Tr. 103; Pet'r Ex. 21 at 5.

In addressing the author's conclusion that this number of cases did not constitute a safety signal, Dr. Andersson noted that the article did not disclose how many cases were discarded because of inadequate data and did not have a defined control group. Tr. 102-05. Dr. Andersson noted that these authors conducted what is called a disproportionality analysis, essentially comparing this vaccine to all other causes of GBS. *Id.* at 105-06. Dr. Andersson noted multiple problems with basing conclusions on VAERS as did the authors. *Id.* at 102-05; Pet'r Ex. 21 at 5. VAERS reporting suffers from multiple problems, particularly underreporting of adverse events possibly related to vaccinations and inadequate detail in some reports. Tr. 102-03, 139. Dr. Andersson testified that GBS is "a very rare syndrome" and that asking a paper based on VAERS to say that there is not a causal relationship between the vaccine and GBS is not appropriate. Tr. 101-03, 149. You need to have better data as to the occurrences and comparisons. *See id.* at 102-03. You cannot assume that every case of GBS after the Prevnar vaccine is included. *Id.* at 102, 139-40. Dr. Andersson said that "he does not accept that the VAERS cases do not represent a signal." *Id.* at 149. He testified that the Haber article uses "back-of-the-shoe-box type…calculations that makes assumptions beyond what the paper shows." *Id.* at 150. He noted that the statistical power of a study to detect rare events such as post vaccinal GBS would have to be very powerful with millions of participants which has not been done. *Id.* at 154.

On cross examination, Dr. Andersson acknowledged that he did not specifically mention the CRM197 mechanism proposed by Dr. Axelrod. Tr. 131. Rather, he stated that his opinion holds open other possible mechanisms by which GBS may be caused. Tr. 130. His report discussed the polysaccharides in the vaccine, but he testified that he was opining that, as the mechanism of GBS has not been fully defined, there are multiple possibilities within the realm of autoimmune disease. *Id.* at 133-34. In discussing which epitopes may cause GBS, Dr. Andersson said that you need "to find some cross-reacting stimulus to an epitope in an axon or myelin that can generate an antibody or cell mediated or even innate response attack to the similar host antigen." *Id.* at 155. He testified that the epitope does not "have to be a saccharide or lipopolysaccharide" and that it "may be a peptide." *Id.* He said his theory was certainly open to the specific mechanism that Dr. Axelrod proposes and he agrees that the mimicry with the CRM197 fits within his concept of potential mechanisms for the triggering of GBS by the Prevnar-13 vaccine. *Id.* at 130-32.

2. Dr. David Axelrod, M.D.

Dr. Axelrod was called by petitioner and was admitted as an expert in immunology. Tr. 173. Prior to the hearing, he authored two expert reports. *See* Pet'r Ex. 29; Pet'r Ex. 45 (ECF No. 52). He opined that more likely than not Ms. Byrd's GBS was caused by molecular mimicry triggered by the immune response to the Prevnar 13 vaccine. Tr. 207-08. Dr. Axelrod testified

that he agreed with Dr. Andersson's theory of molecular mimicry. *Id.* at 174. He defined molecular mimicry as occurring when there are "similar structures or sequences on an environmental agent" which may cause the immune system to cross react to the self-antigens in a susceptible individual and cause them to develop autoimmune disease. *Id.* at 175.

It is his opinion that Guillain Barre syndrome is an autoimmune disease and that it is induced by molecular mimicry based on the available evidence at this time. Tr. 175. He said that for molecular mimicry to occur there must be "similar amino acid sequences between the presumed autoantigen and the environmental agent," but they do not have to be identical. *Id.* at 177. Dr. Axelrod asserted that if there is an amino acid sequence in the foreign pathogen such as in a vaccine or infection that is sufficiently similar to host tissue which is responsible for the disease, molecular mimicry can occur and GBS can be induced. *Id.* at 178.

While he agreed with Dr. Andersson that there are multiple possible mimics between Prevnar-13 and components of the peripheral nerves, he focused his theory on the CRM197 protein to demonstrate a model of molecular mimicry between the vaccine and the peripheral nervous system. *Id.* at 179. The CRM197 protein is conjugated to the sugars in the vaccine in order to increase the immunogenicity of the vaccine. *Id.* at 179. He explained that CRM197 is the diphtheria toxin which, at position 52, substitutes a single glutamic acid for a glycine. *Id.* The deletion of this amino acid renders the diphtheria antigen non-toxic while allowing it to enhance the immune response to the polysaccharides, particularly the serotypes 14 and 18C. *Id.* at 179-80.

The Winer[14]and Wang[15] articles on Guillain Barre Syndrome discussed the likely autoimmune nature of GBS and multiple potential targets of cross reactivity to components of the peripheral nerves, that were referenced by Dr. Axelrod in his testimony. Tr. 185, 199; *see also* Pet'r Ex. 39; Pet'r Ex. 40. Both discussed the role of lipooligosaccharides as demonstrated with post C-jejuni GBS, but, importantly, Wang noted that only a third of GBS cases had been attributed to C-jejuni and only one in 1000 to 5000 C-jejuni patients develop GBS. Pet'r Ex. 40 at 1. Winer discussed mimicry with the P0 and P2 antigens in myelin. *See generally* Pet'r Ex. 39; Tr. 200-201. Other theories postulate mimicry with antigens at the nodes of Ranvier including Contactin-1 and neurofascin. *See* Tr. 199-200.

Dr. Axelrod quoted from a review by Kira et al.[16] in his supplemental expert report in which the authors state that "antibodies against nodal proteins…were detected in a minority of patients" with acute demyelinating disease. Pet'r Ex. 45 at 4; Pet'r Ex. 51 at 1. He also cited to Davies et al.[17] in his report, noting that the authors found antibodies to the following peptides in subjects with Guillain Barre Syndrome:

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[14] J.B. Winer, *An Update in Guillain Barre Syndrome*, Autoimmune Diseases, Jan. 6, 2014.

[15] Ying Wang et al., *Biomarkers of Guillain-Barre Syndrome: Some Recent Progress, More Still to be Explored*, Mediators of Inflammation, Sept. 16, 2015.

[16] Jun-ichi Kira et al., *Anti-neurofascin autoantibody and demyelination*, 130 Neurochemistry International 104360 (2019).

[17] Alexander J. Davies et al., *Immunoadsorption and Plasma Exchange in Seropositive and Seronegative Immune-Mediated Neuropathies*, 9 J. Clinical Medicine 2025 (2020).

1. Neurofascin 186 (NF186) [UniProt Entry: O94856-1]
2. Neurofascin 155 (NF155) [UniProt Entry: H7C0L6]
3. Contactin-1 (CNTN1) [UniProt Entry: Q12860]
4. Contactin-associated protein 1 (CASPR1) [UniProt Entry: P78357]
5. Gliomedin [UniProt Entry Q6ZM13]

Pet'r Ex. 45 at 4; *see also* Pet'r Ex. 52. Dr. Axelrod also referenced an article by Frankild et al.[18] in his supplemental report and his testimony to demonstrate the results of experiments that "amino acid similarity, not identity is a predictive measure of cross-reactivity." Tr. 227-29; Pet'r Ex. 45 at 2; *see also* Pet'r Ex. 46. Building on the concept of T cell degeneracy, developed in Frankild, Dr. Axelrod discussed an article by Hemmer et al.[19] in which the authors reported on experiments with myelin basic protein specific HLA Class II restricted CD4+ T cell clones. Tr. 194; Pet'r Ex. 57. Hemmer states:

> We demonstrated that tripeptides and tetrapeptides can stimulate a CD4+T cell clone and that stimulatory pentapeptides and tetra- peptides may be derived from different segments of the optimal agonist ligand. Interestingly, these short peptides enhanced T cell survival at low antigen concentrations…. These data extend previous views on the minimal requirements for stimulation of CD 4 positive HLA Class 2 restricted T cells and add the dimension of peptide length to T cell receptor degeneracy in recognition of antigen.

Pet'r Ex. 57 at 2. To demonstrate a model of molecular mimicry that could give rise to GBS triggered by the immune response to the Prevnar 13 vaccine, Dr. Axelrod performed a Uni-Prot[20] search which is similar to a Blast search that has been seen in other cases in the program. Tr. 182-83. He explained that, with this search using the alignment function which he did, one puts "in the protein and the species and from that you can get the…right identification number for that protein." *Id.*

He explained that in this search you select a target protein in the database and then another one from the vaccine and use the alignment function to determine if there are similarities between the structures in the vaccine and relevant structures in the peripheral nerves. *Id.* at 183-84. For this case he used the diphtheria toxin as the foreign pathogen which is very close to the CRM 197 conjugate in the vaccine. *Id.* at 185. He chose the CRM 197 because Ms. Byrd did not

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[18] Sune Frankild et al., *Amino Acid Similarity Accounts for T Cell Cross-Reactivity and for "Holes" in the T Cell Repertoire*, 3 PLOS ONE 3 (2007).

[19] Bernhard Hemmer at al., *Minimal Peptide Length Requirements for CD4+ T cell clones – implications for molecular mimicry and T cell survival*, 12 International Immunology 375 (2000).

[20] The UniProt Knowledgebase is a comprehensive, high quality and freely accessible set of protein sequences annotated with functional information. *Uniprot: The Universal Protein Knowledgebase in 2023*, 51 Nucleic Acids Research 523 (2023).

appear to have a cross reaction at least to the saccharides which were tested.[21] *Id.* at 185-86. He looked at the P0 and P2 components of myelin that Winer identified as targets in Experimental Autoimmune Neuritis ("EAN"). *Id.* at 190; Pet'r Ex. 32 at 6, 7. Dr. Axelrod explained that when P0 and P2 were administered to animals they developed EAN. Tr. 201; Pet'r Ex. 40 at 3. Thus, if a foreign antigen has sufficient similarity to P0 or P2 in myelin it can cause a cross reaction and damage the peripheral myelin. Tr. 188-90. In doing the alignment between diphtheria and P0 in myelin, the UniProt search identified a sequence of GRQTPV which had two identical amino acids and four similar ones which Dr. Axelrod opined could be sufficient to stimulate a T cell response in myelin P0 in a susceptible individual. *Id.* at 195-96; Pet'r Ex. 32 at 6.

He then identified a sequence of LGVGLA which was a six amino acid linear sequence that is similar between CRM 197 and myelin protein P2. Tr. 197-98; Pet'r Ex. 32 at 7. Using the UniProt alignment tool Dr. Axelrod also identified multiple potential mimics between CRM 197 and different nodal and paranodal antigens that are theorized to be targets in a subset of patients fulfilling GBS diagnostic criteria. Tr. 198-99; Pet'r Ex. 32 at 5. In his expert report, Dr. Axelrod cited to a 2021 article by Querol and Lleixa that pointed to antibodies to neurofascin 140/186, neurofascin 155, CASPR1 and Contactin 1 as being likely targets in GBS.[22] Pet'r Ex. 29 at 5; s*ee also* Pet'r Ex. 34 at 8. These authors wrote:

> As found in CIDP, a subset of patients fulfilling GBS diagnostic criteria also associate with antibodies against nodal and paranodal proteins (neurofascin 140/186, neurofascin 155, CASPR1, and contactin 1). Most of them are aggressive presentations of autoimmune nodopathies that respond poorly to conventional GBS therapies; a few remain monophasic and respond to intravenous immunoglobulins.

Pet'r Ex. 34 at 8. Dr. Axelrod, through his UniProt search, found sequences of the same or conserved similar amino acids of 3-5 or 3-6 in alignment between diphtheria and multiple antigens most importantly for neurofascin 155, Contactin 1, and CASPR1. *See* Pet'r Ex. 34.

On questioning by the court, Dr. Axelrod agreed that, in the literature on GBS, it is "frequently postulated that whether the prior condition was an infection" or vaccination that molecular mimicry is a likely cause of GBS. Tr. 241. He also agreed that it is "likely that molecular mimicry is a starting point" of a reaction in a susceptible person and that there is a failure of tolerance and or of the regulatory system which are likely co-actors in the development of an autoimmune disease such as GBS. *Id.* at 241-42. As noted, the vast majority of people who get C-jejuni do not develop GBS which strongly suggests that other components of the immune system are involved in causing the disease when a cross reaction is triggered by that bacterium. *Id.* Dr. Axelrod testified that Ms. Byrd was a susceptible individual and developed GBS, triggered by the vaccine, which her immune system failed to regulate. *See id.* at 234-35.

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[21] On the ninth day of her hospitalization, Ms. Byrd's tests demonstrated significantly elevated complement CH50 at 229, but her ganglioside panel was negative with the following values: GM1:27, GD1A ab:25, GD1B ab:29. Values of 30-50 are considered equivocal and 51-100 are considered positive. Pet'r Ex 6 at 237.

[22] Luis Querol & Cinta Lleixa, *Novel Immunological and Therapeutic Insights in Guillain-Barre Syndrome and CIDP*, 18 Neurotherapeutics 2222 (2021).

i. Respondent's Experts

1. Peter Donofrio, M.D.

Dr. Peter Donofrio was called by the respondent and admitted as an expert in neurology. Tr. 256. Dr. Donofrio primarily focused on studies reporting on cases of GBS following Prevnar or epidemiology. *Id.* at 258-59. He first addressed the Haber report, also discussed by petitioner's experts. *Id.*; Pet'r Ex. 21. Haber, using VAERS data found 11 post Prevnar cases of GBS, eight of which it accepted for the report. Pet'r Ex. 21 at 4. Over the time period of the study, from 2012-2015, Haber reported that there were about 16 million doses of Prevnar given in the 3.5-year period of the study. *Id.* Dr. Donofrio testified that most people would agree that about 10 to 30 cases of GBS per million people occur annually from all causes, and thus, he would have expected a background rate of 45 to 100 cases over the period of the study. Tr. 258-60. He noted that the Haber authors calculated a rate of "0.7 cases per million compared to the baseline rate of what we already talked about, 10 to 30 per million population" and that the authors concluded that "there was no relationship between the Prevnar 13 vaccination and the development of GBS." Tr. 261. Dr. Donofrio agreed with the authors conclusion that there was no safety signal or increased incidence of GBS. *Id.* at 262. He acknowledged that VAERS data is woefully underreported and noted that Haber was not an epidemiological study but rather "a description of the results of reports to the VAERS system." *Id.* at 280. Dr. Donofrio also agreed that such underreporting skews the results of the report. *Id.* at 281.

Respondent's counsel next directed Dr. Donofrio's attention to the Tseng study.[23] Resp't Ex. C, Tab 11 at 7; Tr. 262. This study compared adverse events following administration of Prevnar 13 to administration of the older PPSV23 vaccine. Tr. 263; Resp't Ex. C, Tab 11. The study concluded that there was not a significantly increased risk of GBS following Prevnar 13 compared to the PPSV23. Tr. 264.

He also discussed the Bonten study.[24] Resp't Ex. C, Tab 13; Tr. 265. This was a double-blind study to primarily compare the efficacy of Prevnar to PPSV23. Tr. 265-66. The article briefly discussed adverse events in general and Dr. Donofrio testified that "the authors stated that…there was no increased incidence of GBS in patients who received Prevnar 13." Tr. 266. The petitioner established on cross examination that this study does not mention GBS and that it was funded by Pfizer, the manufacturer of the vaccine. *Id.* at 278. Dr. Donofrio said it is likely that they would have included GBS occurrences within the general category of adverse events but agreed that the primary focus of the study was on the comparative immunogenicity of the two vaccines. Dr. Donofrio testified that double-blind studies are superior to case reports, and he concluded that there was no epidemiological evidence to support a connection between Prevnar and GBS. *Id.* at 266-69. He also observed, as did Dr. Axelrod, that the reports on S-

[23] Hung Fu Tseng et al., *Pneumococcal Conjugate Vaccine Safety in Elderly Adults*, Open Forum Infectious Diseases, Jun. 2018.

[24] M.J.M. Bonten et al., *Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults*, 372 New England J. Medicine 12 (2015).

pneumonia infections would not shed light on the CRM 197 element of the petitioner's theory as CRM 197 is not a component of the wild disease. *Id.*

Referring specifically to petitioner, he noted that she tested negative for several anti-ganglioside antibodies, but she was not tested for anti-myelin antibodies. Tr. 270. He did agree with the diagnosis of GBS and agreed that GBS is an acquired autoimmune disease. *Id.* at 273, 281. He also agreed that Ms. Byrd was in good health prior to receiving the vaccination and that anyone who could swim a mile three times a week and was generally active was probably in good health. *Id.* at 272-73. She had no indicia of GBS prior to February 10, 2019. *Id.* Dr. Donofrio agreed that he was not offering an opinion on whether timing was appropriate in petitioner's case "because [he] does not think there is a causal link at all between Prevnar 13 and GBS." Tr. 282.

Dr. Donofrio testified that he was familiar with the animal model EAN referenced above and that the model provides a proposed mechanism for molecular mimicry, but he indicated that "there has to be a specific trigger to the immune system," and not "just a global increase in the immune system." Tr. 274. He also agreed that molecular mimicry is accepted in the medical community as one potential cause of GBS. *Id.* Finally, Dr. Donofrio agreed that in someone who contracts a severe case of GBS, such as the petitioner did , the acute phase can go on to have very significant permanent problems and that petitioner's case "is a severe case of disability following [her] GBS diagnosis." *Id.* at 281-282.

2. Lindsay Whitton, M.D., Ph.D.

Dr. Whitton was presented by respondent and admitted as an expert in immunology. Tr. 300. Dr. Whitton opined that he does not "think that reliable scientific evidence supports the notion that Prevnar 13 can trigger GBS," and he applies that conclusion to this case. *Id.* at 301. He explained that streptococcus pneumoniae is equivalent to pneumococcus in terminology. *Id.* He explained the structure of the streptococcus pneumoniae bacterium with particular reference to its outer polysaccharide capsule, which he said is the most relevant aspect of its structure to this case. *Id.* at 302. The bacteria are surrounded by a "waxy cell wall, which is made up largely of polysaccharides, which are long sugar molecules." *Id.* He further explained that "some of these sugar molecules…have chemically attached small molecules such as phosphoglycerol." *Id.*

Dr. Whitton explained that polysaccharides are composed of a chain of single molecules of sugar, called monosaccharides. Tr. 303. The term "polysaccharide" is "applied to chains that exceed 12 monosaccharides." *Id.* There are a wide range of monosaccharides in nature and the monosaccharides in the chain can combine in different ways and branch out to create different polysaccharides. *Id.* at 303-04. While "there are a large number of polysaccharides in nature, the number of possible combinations is not limitless because it is constrained by the fact that there are only a relatively small number of enzymes that are capable of generating these different linkages." *Id.* at 304. He went on to indicate that there are different polysaccharides in the S-pneumoniae bacterium capsules and that each different polysaccharide will generate a different antibody response which is unique to itself. *Id.* at 304-05. The particular strain of bacteria is called a serotype, which is based on the serological response that is mounted to the bacteria. *Id.*

at 305. He said that the antibody responses are" not really cross-reactive" (as to different strains of the bacteria) allowing the typing of "roughly 100 different strains of strep pneumoniae." *Id.*

Dr. Whitton went on to discuss that Prevnar 13 was developed because the Pneumovax 23 did not work well in infants. Tr. 306. To "overcome the reluctance of the infant immune system," the pneumococcal antigens were conjugated, or chemically combined with, CRM 197, which is the diphtheria toxin less one amino acid to render it non-toxic. *Id.* at 307. The CRM 197 elicits a T cell response most of which are CD4 T helper cells which "secrete cytokines that provide help to specific B cells…to turn on antibody production against the polysaccharides." *Id.* at 308.

He agreed that GBS is broadly accepted as autoimmune, and testified that his opinion at the moment, is that some forms of GBS, such as AMAN and AMSAN are clearly autoimmune and need to involve molecular mimicry. Tr. 308-09. He said he is on the fence about whether other forms of GBS are caused by molecular mimicry as autoimmunity can be induced by means other than molecular mimicry. *Id.* He discussed that one strain, the 019 strain, of C-jejuni has been shown to cause GBS. *Id.* at 332. He explained that C-jejuni is a gram-negative bacterium, meaning it has a thin membrane surrounding it made of lipooligosacchrides and it is this component in the 019 strain that is thought to cause GBS after a C-jejuni infection. *Id.* at 331–34. S-pneumonia, on the other hand, is a gram-positive-bacteria and as such does not have the thin lipooligosacchride membrane surrounding it. *Id.*

Dr. Whitton agreed that in the great majority of cases autoimmunity is triggered by an exogenous source such as infection or vaccination. Tr. 341. However, he argued that "theoretically, you don't need to have an exogenous trigger of disease." *Id.* at 342. There could be some change in T cells that renders a person more susceptible than another might be. *Id.* at 342-44. So, he concluded that there is no absolute need for an exogenous trigger, but he did agree that some autoimmune diseases are triggered by an exogenous stimulus. *Id.* at 344. He discussed the tolerance system and the body's negative selection of T cells that might attack self. *Id.* at 345. He also agreed that the causation of autoimmune diseases is likely multi-factorial potentially involving molecular mimicry, the failure of tolerance and a failure of the regulatory system although he was not sure about the role of T cell degeneracy. *Id.* at 339–40.

Dr. Whitton was asked whether he thought any vaccine could cause GBS. Tr. 325. He answered that as to the swine flu vaccine he could not argue with the data of Langmuir and Schonberger, but other than that one vaccine, he did not think that the evidence was strong for vaccine causation of GBS, and he did not think it was strong for Prevnar 13. *Id.* at 326. He then clarified that he thought some vaccines could cause GBS very rarely. *Id.* at 327. He said that in his mind, there is no evidence that strep pneumoniae can cause GBS and so he did not think the polysaccharides in Prevnar 13 can cause GBS. *Id.* at 329.

Respondent's counsel then turned Dr. Whitton's attention to Dr. Axelrod's theory of mimicry between CRM197 and several components of the peripheral nerves. Tr. 345-46. After noting that case reports involving S. pneumonia infection do not support mimicry with CRM197, which Dr. Axelrod had acknowledged because CRM 197 is not present in the wild disease, Dr. Whitton agreed that some of the structures that Dr. Axelrod identified in his UniProt search

could be bio-markers of GBS. *Id.* at 346-48. However, he argued that this did not necessarily imply causation and that some of the antibodies could be generated as a result of disease rather than the cause. *Id.* at 348. Dr. Whitton questioned whether short three amino acid peptides could be sufficient to stimulate a T cell response. *Id.* at 350. He acknowledged that T cells are very sensitive when peptides are presented on MHC[25] complex molecules. *Id.* at 351-52, 354-56. He indicated, without differentiating between MHC1 and MHC2 molecules, that somewhere around 8-15 amino acids being presented by an MHC molecule on the surface of a cell would be sufficient to stimulate a T cell response. *Id.* at 352-53. He talked about the Hemmer paper, noting that they were able to stimulate T cell response in a petri dish by pouring "the epitopes onto the outside of the cell" rather than inside a cell. The epitopes were "in the form of synthetic peptides" and he argued that the study was able to stimulate the T cell response to short peptides because of "the number of synthetic peptides that" the study used. Tr. 353-55; *see* Pet'r Ex. 57. Dr. Whitton responded to Dr. Axelrod's use of a paper authored by Dr. Whitton "for the proposition that cytotoxic T lymphocytes could be activated by a small peptide of five amino acids in length." Tr. 357; Pet'r Ex. 56 at 6.[26] Although the paper, as published, reported on the generation of cross reactivity of cytotoxic T cells when stimulated by a 5 amino acid peptide, Dr. Whitton, at the hearing, asserted that they were only able to do that by utilizing large quantities of the peptides in question. Tr. 358-62. He testified that the study looked at two closely related viral peptides, the ARM and the Pasteur, and the T cells readily responded to their cognate antigen. But the ARM T cells did not respond to the Pasteur antigen until they increased the amount of Pasteur peptide by fourfold. *Id.*

When commenting on the Frankild article, Dr. Whitton agreed that similarity is more important than identity in terms of molecular mimicry, as the foreign antigen must be different or non-identical in order to provoke the immune response. Tr. 363-65. However, he said that showing similarity does not predict cross reactivity, which he said can only be done with experiments. *Id.* at 365. Dr. Whitton opined that Dr. Axelrod's conclusion that, more likely than not, the Prevnar 13 vaccine can cause GBS was not a scientifically reliable conclusion. Tr. 371.

Dr. Whitton agreed on cross examination that molecular mimicry "boils down to a foreign material, either an infectious organism or vaccine, [that] contains a sequence within it that is sufficiently similar to a sequence in a host molecule" and that the foreign antigen must be "sufficiently similar that the immune response will mistakenly target the host material, whether it is a ganglioside, phospholipid, protein or something else." *Id.* at 380. Dr. Whitton then refined that answer as it relates to the development of GBS to say that the similar sequence must be "sufficiently immunologically similar" not just chemically similar and that the host tissue to which it is similar must be tissue that is responsible for the development of the disease. *Id.* at 381-82.

Referring to a prior answer in which Dr. Whitton indicated that the swine flu vaccine was epidemiologically linked to GBS in the past, petitioner's counsel asked what the mechanism of injury was for that vaccine, which Dr. Whitton acknowledged seems to have triggered GBS. Tr. 383. Dr. Whitton responded that he did not know, but that molecular mimicry was one possible

[25] MHC stands for Major Histocompatibility Complex.

[26] J. Lindsay Whitton et al., *Molecular Analyses of a Five-amino-Acid Cytotoxic T-Lymphocyte (CTL) Epitope: an Immunodominant Region Which Induced Nonreciprocal CTL Cross-Reactivity*, 63 J. Virology 4303 (1989).

mechanism and that "broadly speaking most people remain puzzled as to why that swine flu vaccine actually did what it seems to have done with regard to causation of GBS." *Id.* He agreed that molecular mimicry was at least suspected as the mechanism for the swine flu vaccine and GBS. *Id.* at 384. Dr. Whitton testified that he is not aware of any other vaccines that have been *clearly* shown to trigger GBS. *Id.* at 383. He acknowledged that there are vaccines for which GBS was reported in an appropriate timeframe and some including Prevnar 13 where GBS is mentioned in the package insert but he said that is not proof of causation and he is not aware of any other vaccines about which we can *confidently* assert that they were the trigger. *Id.* at 384.

Dr. Whitton was asked about molecular mimicry in the case of *C. jejuni*. Tr. 385. Dr. Whitton emphasized that he did not want to say that the 019 strain was the only one that could have mimicry with peripheral nerves or that *C. jejuni* was the only possible source of molecular mimicry. *Id.* He said in the case of *C. jejuni* he would not use the terms homology or sequence similarity because you are talking about saccharides and gangliosides. *Id.* at 386. He preferred to call it structural similarity whereas the terms homology and sequence similarity generally refers to proteins. *Id.* at 387.

Dr. Whitton acknowledged that EAN has been used as a peripheral nerve model and agreed that, as reported in the Winer article, they were able to induce EAN in the lab through P0 and P2. Tr. 389-93. He agreed that EAN has been used as an animal model for GBS but because of how these laboratory experiments are done, he did not think that EAN and GBS are identical. *Id.* He did agree that T cell lines reacting with P2 in myelin can transfer the disease from one subject to another and that leads to the inescapable conclusion that P2 is at least in part responsible for EAN as shown in the Winer paper. *Id.* at 391. He said that there was enthusiasm after these EAN experiments that P0 and P2 would be an important target in GBS. *Id.* at 392. But when others looked at people with GBS to see if they could find strong responses to P0 and P2 generally speaking they could not. *Id.* He did however, note that he was not saying that P0 and P2 are not involved in GBS, he was just saying that to the best of his knowledge there is not *strong* evidence that P0 and P2 are pathologic targets in GBS. *Id.* at 392-93. He said that he did not know if P0 and P2 were biomarkers for GBS but acknowledged that they were listed as biomarkers of the syndrome in the Wang paper. *Id.*

When asked about how long he thought a peptide would have to be to have structural similarity for cross reactivity to occur, he said this is a very difficult question but said that most epitopes that generate T cell responses "are somewhere around eight or nine amino acids at the shortest and 50 [sic] or 60 [sic] at the longest."[27] He also noted that "you can get 20 amino acid long epitopes" for CD4 T cells. Tr. 395-96. He argued that he is not aware of any studies in terms of actual immunology involving infection or vaccination where you would get very many responses to peptides shorter than eight or nine. *Id.* at 396. Counsel then quoted to him an explanatory sentence from the Kanduc study[28] which said, "We used the 5-mer sequences as probes to scan viral human proteins against human proteomes, since pentapeptides are minimal

[27] I suspect that this reference to 50 or 60 was incorrectly transcribed in the hearing transcript and that the actual testimony was 15 or 16.

[28] Dajara Kanduc et al., *Massive peptide sharing between viral and human proteomes*, 29 Elsevier 1755 (2008).

structure units critically involved in biological/pathological interactions, such as peptide protein interaction and autoimmune recognition." Pet'r Ex. 58 at 3; Tr. 398-99. Dr. Whitton noted that he did "not necessarily agree with what is written." Tr. 399. However, Dr. Whitton also noted that he had not looked closely at the referenced cited in the study supporting the statement. *Id.*

The testimony then focused on Prevnar 13 specifically. Tr. 399-404. Dr. Whitton agreed that there are three parts of Prevnar 13 that can be recognized by the immune system — the polysaccharides, CRM197, and the alum adjuvant. *Id.* at 399-400. He agreed that CRM197 was included to heighten the immune response at least in infants, though he is "not sure there is *hugely strong* evidence that it heightens the immune response in adults." *Id.* (emphasis added). Dr. Whitton agreed that, after vaccination with Prevnar 13, memory T cells are produced that are anti-CRM197. *Id.* at 401. He agreed that if these T cells can recognize a host structure, and GBS develops then you could have a molecular mimic, but qualified this by stating that recognition was a "big assumption." *Id.* at 401-02.

Dr. Whitton was asked about testimony he gave in another Prevnar 13/GBS case where he said that if Prevnar were to trigger GBS he thinks it would be more likely through the CRM197 than the polysaccharides. Tr. 402-03. He based this opinion on "the fact that there is no known association between pneumococcus, strep pneumoniae, and GBS" and asserted that "if the polysaccharides triggered GBS via molecular mimicry, then one would predict that there would be…a known, demonstrable association between the bacterial infection and GBS." *Id.*at 403. Thus, "if Prevnar were to trigger GBS," which Dr. Whitton disputes, he believes that it is "more likely to be through CRM197," which is in the vaccine but not in the wild bacteria. *Id.* Dr. Whitton maintained that he does not believe there is "reliable evidence that Prevnar 13 can trigger GBS" and noted that he would not move from this opinion without information convincing him otherwise. *Id.* at 402.

In concluding his testimony, Dr. Whitton agreed that, in order for him to agree that molecular mimicry caused the disease, "the proposed mimic has to actually be recognized by the immune system," then "the circulating autoantibody actually attacks the host tissue through the cross-reactivity," then "you have to have resulting disease," in this case, GBS. Tr. 406-07. However, Dr. Whitton argued that he does not believe petitioner has shown structural similarity, and, rather, has only showed chemical similarity between antigens in Prevnar-13 and potentially relevant host antigens such as P0 and P2 in myelin or Contactin1 in the paranodal areas. Tr. 407-08. The fact that Dr. Axelrod was able to show short homologies between the vaccine and multiple potential targets in the peripheral nerves is just a function of the fact that "whenever you take two average length proteins…you will always find multiple homologies, every time." *Id.* at 408. However, Dr. Whitton agreed that Prevnar 13 was, as far as we know, the only known immune provocation in the appropriate time period in petitioner's case. *Id.* at 414. He reverted to his argument that autoimmune diseases have an alternative possibility where a specific exogeneous stimulus is not needed "because of the fact that your immune system is constantly pouring out these T cells, some of which are potentially capable of causing autoimmune disease without any provocation." *Id.* However, he admitted that there is no evidence of a T cell malfunction in petitioner's case and that the only known immune stimulus within the appropriate time frame in Ms. Byrd was the Prevnar vaccine. *Id.* at 414-15.

III. LEGAL STANDARD

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" *Rooks v. Sec'y of Health & Hum. Servs.*, 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs*., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *see also Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, "that the vaccinee's injury is due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

To receive compensation through the Program, petitioner must prove either (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that he suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Because petitioner in the present case does not allege that she suffered a Table Injury, she must prove that the vaccine she received caused her injury. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and her injury ("*Althen* Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for her injury ("*Althen* Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and her injury ("*Althen* Prong Three"). § 13(a)(1); *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548-49 (Fed. Cir. 1994). The Federal Circuit has reiterated that proof of causation does not "require identification and proof of specific biological mechanisms[.]" *Kottenstette v. Sec'y of Health & Hum. Servs.,* 861 Fed. Appx. 433 (Fed. Cir. 2021) (citing *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)). Causation "can be found in vaccine cases….without detailed medical and scientific exposition of the biological mechanisms." *Knudsen,* 35 F.3d 543, 548-49 (Fed. Cir. 1994). It is not necessary for a petitioner to point to conclusive evidence in the medical literature linking a vaccine to the petitioner's injury, as long as the petitioner can show by a preponderance of evidence that there is a causal relationship between the vaccine and the injury, whatever the details of the mechanism may be. *Moberly*, 592 F.3d at 1325 (Fed. Cir. 2010). The petitioner need not make a specific type of evidentiary showing such as "epidemiologic studies, rechallenge, the presence of

pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. *Id.* at 1325-26.

Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any…conclusion, [or] medical judgment…which is contained in the record regarding…causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in his favor. *See Moberly*, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); *Althen*, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

In Vaccine Act cases, expert testimony may be evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993); *see also Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). In Vaccine Program cases, the *Daubert* analysis has been used in the weighing of the scientific evidence actually proffered and heard rather than as a tool for the pre-trial exclusion of expert testimony. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"), *aff'd*, 420 F. App'x 923 (Fed. Cir. 2011). The flexible use of the *Daubert* factors to determine the persuasiveness and/or reliability of expert testimony in Vaccine Program cases has routinely been upheld. *See, e.g.*, *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 742-45 (2009).

Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1362 (Fed. Cir. 2000)). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280 (holding that Congress created a system in which "close calls regarding causation are resolved in favor of injured claimants"); *Knudsen*, 35 F.3d at 551 ("If the evidence (on alternative cause) is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded.").

IV. Analysis

There is agreement between the parties on the basic facts of the case. The petitioner received the Prevnar 13 vaccine on February 6, 2019 at the office of her family physician in Albuquerque, New Mexico. The parties agreed that the petitioner appeared to be in good health at that time. They also agreed that she was subsequently correctly diagnosed with Guillain Barre syndrome, and that the onset of her illness began approximately four days after she received the Prevnar vaccine. Her symptoms began with pain in her ankles on February 10 for which she went to the emergency department but was sent home with a diagnosis of anxiety. Beginning on February 13, her pain became worse. On the evening of the fifteenth, she began to develop weakness in the lower extremities. She fell multiple times by the following day when her neighbors called an ambulance to transport her to Lovelace Medical Center. She was admitted to the hospital on February 16. Her condition deteriorated very rapidly over the next several days to extreme weakness in all extremities with compromised breathing for which she was intubated. She also experienced facial symptoms including weakness and ptosis. It was also agreed that GBS is an autoimmune disease that in this case has been and remains severely disabling. The respondent's experts agreed that there were no known alternative causes of her illness and that the Prevnar 13 vaccine was the only known immune stimulant that the petitioner received within the weeks prior to the onset of her illness. Thus, the only issue for determination is whether the Prevnar-13 vaccine petitioner received caused her GBS.

a. *Althen* Prong One

Under the first prong of *Althen,* a petitioner must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56. To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Proof of causation does not "require identification and proof of specific biological mechanisms[.]" *Id.* at 549. "It is not necessary for a petitioner to point to conclusive evidence in the medical literature linking a vaccine to the petitioner's injury, as long as the petitioner can show by preponderance of the evidence that there is a causal relationship between the vaccine and the injury, whatever the details of the mechanism may be." *Moberly v. Sec'y of Health & Human Servs.,* 592 F.3d 1315, 1325 (Fed. Cir. 2010).

The petitioner posited a theory of molecular mimicry between the Prevnar 13 vaccine and the peripheral nervous system as the cause of her very severe GBS. Dr. Andersson approached causation from the point of view of neurology and correctly noted that much has been written about GBS, that it is generally agreed that GBS is an autoimmune condition, and that the specific causes of the autoimmunity are not well understood. This view is consistent with the array of articles on GBS filed by both parties such as Winer, Wang, Goodfellow, Willison, and others

that describe the efforts to come to a definitive understanding of the immune response that causes GBS. However, these authors uniformly expressed the frustration of the medical community about the failure of scientific research to fully explain the causation of GBS despite much research. While much literature points to prior infections as possibly causal in many cases of GBS, the literature also recognizes the potential role of vaccines in giving rise to autoimmune disease, including GBS through molecular mimicry or other mechanisms. The literature also recognizes that the vast majority of people who have identified respiratory or gastrointestinal illnesses or vaccinations do not develop autoimmune diseases.

The parties' experts discussed *C. jejuni*, a gram-negative bacterium that has a thin peptidoglycan membrane that has been shown to precede GBS in close to a third of cases but not in the others. Mimicry between this lipopolysaccharide membrane in *C. jejuni* and several of the gangliosides in peripheral nerves appears to be accepted as well. Strep pneumoniae is a gram-positive bacterium with a peptidoglycan cell wall that is substantially thicker than that in the gram-negative bacteria. While mimicry between the gram-negative membrane in at least one strain of *C. jejuni* has been accepted, potential mimicry between components of the gram-positive Strep pneumonia bacteria such as the thick peptidoglycan wall surrounding it has not been ruled in or out, similarly to most molecular causes of GBS.

Dr. Andersson described that the antibody or cellular response to a cognate antigen in the peripheral nerves is thought to stimulate an antibody or T cell directed immune response causing the deposition of complement at the nodes of Ranvier which is destructive of the target in the peripheral nerve and triggers some degree of cell mediated toxicity. Macrophages then come in and cause further damage. It is notable that Ms. Byrd's general complement level (CH50) was significantly elevated at 229 (Ref. range 60-144) when measured on February 17. An article by Kaida[29] submitted by petitioner reads that:

> Recent studies have revealed that the nodes of Ranvier are the main target regions in pathophysiology in GBS, especially AMAN. Autopsy studies and analyses of rabbit models sensitized with gangliosides have shown that deposits of activated complement and disruption of clusters of voltage gated sodium channels are observed only at the nodes.

Pet'r Ex. 35 at 15. Dr. Andersson testified that his opinion provided a general description of the thinking as to the potential causes of the autoimmune response in GBS. He said that he described the polysaccharides, and that his theory also includes the CRM197 theory more specifically developed by Dr. Axelrod. As noted above, CRM197 is not present in the wild bacteria and thus creates a second potential source of mimicry between the vaccine and peripheral nerves as theorized by Dr. Axelrod. Dr. Whitton agreed that the immune system reacts to the sugars, to CRM197, and to the adjuvant in the vaccine.

Dr. Axelrod testified that the literature on GBS frequently posits molecular mimicry as the likely starting point of a reaction in a susceptible person and that there is a failure of tolerance and/or the regulatory system which are likely co-actors in the development of this autoimmune disease. As such, Dr. Axelrod opined that the pathogenesis of GBS is very likely to be multi-

[29] Kenichi Kaida, *Guillain Barre Syndrome,* 1190 Advances in Experimental Medicine and Biology 323 (2019).

factorial, with which Dr. Whitton agreed. *See* Tr. 344-45. He opined that, more likely than not, molecular mimicry between the Prevnar vaccine and components of the peripheral nerves in combination with a susceptibility in petitioner and a failure of the other protective mechanisms such as the regulatory system acted in concert to cause her GBS.

Dr. Andersson discussed the potential for mimicry between the polysaccharides in the vaccine and the saccharides in the peripheral nerves and between the protein components of CRM197 and the nerves. Dr. Axelrod focused on the potential protein mimicry between the diphtheria conjugate in the vaccine known as CRM197. He initially focused on the P0 and P2 molecules in peripheral nerve myelin as they had been referenced as likely targets in the Winer article. He found acceptable mimicries between peptides in the vaccine and in both P0 and P2. Significantly, he also identified acceptable mimics between Contactin1, CASPR1, and neurofascin which are also thought to be targets in the nodal and paranodal areas and may be particularly relevant in axonal GBS as these proteins are thought to play a crucial role in maintaining saltatory conduction.[30] This mimicry is likely important in this case as the treating neurologist at Lovelace Hospital opined that petitioner's GBS was "most consistent with severe GBS the axonal motor subtype clinically." Pet'r Ex. 6 at 242. Further, Dr. Whitton testified that the AMAN and AMSAN[31] forms of GBS particularly need to involve molecular mimicry. Tr. 309.

Dr. Axelrod explained that, following the initiation of the immune cross reaction with the peripheral nerve components in an individual who is susceptible comes a failure of tolerance as well as a likely failure of the T-regulatory system to tamp down or eliminate the cross-reactive response to the immune stimulus, in this case the Prevnar vaccine. Dr. Axelrod opined that the Prevnar vaccine was likely the trigger, probably through response to the CRM197, but potentially also to gangliosides and that petitioner's condition advanced rapidly to the severe level it did through a multi-factorial immune system failure after the initial cross reaction. Tr. 241-42. Dr. Andersson referred to an illustration from Goodfellow, which demonstrated the theory of antibody driven attack by complement and macrophages on the myelin and these critical proteins in the nodal and paranodal region of the peripheral nerves in the generation of

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[30] The Kira article described experiments in mice which demonstrated the importance of neurofascin, Contactin 1 and CASPR1 in the peripheral nerves. "Glial NF155 is expressed at the paranodal loops of oligodendrocytes in the CNS (Tait et al., 2000) and in Schwann cells in the PNS (Sherman et al., 2005). Glial NF155 interacts with axonal CNTN1 and CASPR1 (Pedraza et al., 2001). In NF-null mice, transgenic expression of NF155 in the myelinating glia recruits CNTN1 and CASPR1, restoring the axonglial adhesion complex at the paranodes. However, clustering of sodium channel and NrCAM at the nodes was not recovered (Sherman et al., 2005), suggesting a crucial role of NF186 in assembling the nodal complexes. Glial NF155 forms septate-like transverse bands between terminal loops and axons together with axonal CNTN1 and CASPR1 to maintain the ion channel clustering at nodes of Ranvier (Sherman et al.,2005). Myelinating glia-specific ablation of NF155 caused marked reduction of nerve conduction velocity together with migration of paranodal CASPR1 and juxtaparanodal potassium channels (Kv1.1) toward the nodal region (Pillai et al., 2009), suggesting that NF155 is indispensable for separating nodal voltage-gated sodium channels from juxtaparanodal potassium channels. As loss of NF155 and CNTN1 in genetically modified mice leads to disruption of septate-like junctions, leaving a large gap between the axolemma and Schwann cell terminal loops, which decreases nerve conduction velocity (Boyle et al., 2001; Sherman et al., 2005; Pillai et al., 2009), these molecules are regarded as fundamental to maintain saltatory conduction." Pet'r Ex. 51 at 3.

[31] AMAN refers to the axonal motor form of GBS and AMSAN to the axonal motor sensory form.

GBS. Pet'r Ex. 12 at 6. Respondent submitted similar articles and illustrations such as Willison,[32] which indicated that "an important body of evidence has proven that anti-ganglioside antibodies exert their paralytic effects directly. Nevertheless, tissue bound antibody of the appropriate class should automatically fix complement that would therefore exacerbate injury over and above any direct actions of the antibody." Resp't Ex. A Tab 7 at 9.

In petitioner's case three anti-ganglioside antibodies were tested about 15 days after onset and, while not zero, they were slightly less than the level the lab rated as equivocal. On the other hand, her CH50 general complement test was well above the normal range at the same time. Antibodies to the other gangliosides frequently mentioned in connection with GBS do not appear to have been tested. There was no disagreement among the parties that there was no known other immune stimulant beside the vaccine in the weeks or months before onset of her GBS.

Dr. Axelrod submitted an article by Rojas,[33] which observed that "One of the leading mechanisms by which infections or chemical agents may induce autoimmunity is molecular mimicry, which occurs when similarity between foreign and self-peptides favor an activation of autoreactive T or B cells by foreign-derived peptides in a susceptible individual." Pet'r Ex. 60 at 1. Rojas further observed that it has been suggested "that the homology between the human proteome and the adjuvanted-vaccines in a genetically susceptible host may increase the possibility for the induction of cross-reactive immune responses that lead to autoimmune disease." *Id.* at 3. As noted above, many of the articles filed in this case discuss the likelihood of molecular mimicry as a causal mechanism in the development of GBS.

While Dr. Donofrio and Dr. Whitton contended that there is not *strong evidence* that Prevnar 13 can cause GBS, Dr. Donofrio mostly referred to the small number of epidemiological reports, including Haber, Tseng and Bonten that either reported on small surveys, as in Haber, or on a comparison between Prevnar and PVC23. He did agree that the Haber study was not an epidemiological study but rather just a description of data reported to VAERS, which data he agreed are woefully underreported. Tr. 280-81. Dr. Donofrio also agreed that Ms. Byrd's diagnosis is GBS and that GBS is generally thought to be an autoimmune disease.

Dr. Whitton argued that he did not think that the wild strep pneumoniae bacteria causes GBS and therefore, if there was evidence that the Prevnar vaccine caused GBS, that it would more likely be because of mimicry with the CRM197 protein conjugate as proposed by Dr. Axelrod. He discussed the multiple papers that were filed by petitioner in support of short peptide homologies between CRM197 and various components of the peripheral nerves and generally criticized cross reactivities between nerve proteins and the short peptides as being primarily the result of the methodology applied in the laboratory experiments.

In short, Dr. Whitton repeatedly noted that he did not think there was strong, robust, or convincing evidence that the Prevnar vaccine or for the most part any other vaccine could cause GBS by molecular mimicry. I understand his desire as a scientist to have definitive or nearly definitive epidemiological or mechanistic evidence of vaccine causation before accepting same.

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[32] Hugh Willison, *The immumobiology of Guillain-Barre syndrome*, 10 J. Peripheral Nervous System 94 (2005).

[33] Manuel Rojas et al., *Molecular Mimicry and autoimmunity*, 95 Journal of Autoimmunity 120 (2018).

However, given that such conclusive evidence does not exist in medicine, this is not the burden of proof required of the petitioner in Vaccine Program cases. Petitioners are not required to demonstrate a specific biologic mechanism by which their disease is caused, nor are they required to provide epidemiological studies in support of their theory. *See Kottenstette v. Sec'y of Health & Hum. Servs.*, 861 Fed. Appx. 433 (Fed. Cir. June 15, 2021) (cititng *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d at 549 (reaffirming the principle that "proof of causation does not 'require identification and proof of specific biological mechanisms[.].'")); *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d at 1378-79.

Molecular mimicry has been accepted in the Vaccine Program as a sound and reliable theory to explain how vaccines can cause GBS and other neurologic conditions. *See e.g., Stitt v. Sec'y of Health & Hum. Servs.,* No. 11-140V, 2013 WL 3356791, at *8-9 (Fed. Cl. Spec. Mstr. May 31, 2013) (finding petitioner's biological mechanism of molecular mimicry demonstrated that the flu vaccine could cause GBS); *Roberts v. Sec'y of Health & Hum. Servs.*, No. 09-427V, 2013 WL 5314698 (Fed. Cl. Spec. Mstr. Aug. 29, 2013) (finding that Tdap vaccine led petitioner to develop transverse myelitis via molecular mimicry); *Salmins v. Sec'y of Health & Hum. Servs.*, No. 11-140V, 2014 WL 1569478 (Fed. Cl. Spec. Mstr. Mar. 31, 2014) (finding that HPV vaccine caused petitioner to develop GBS via molecular mimicry); *Spayde v. Sec'y of Health & Hum. Servs.*, No. 16-1499V, 2021 WL 686682 (Fed. Cl. Spec. Mstr. Jan. 27, 2021) (finding that molecular mimicry is a sound and reliable theory for the influenza vaccine to cause GBS); *Reinhardt v. Sec'y of Health & Hum. Servs.*, No. 17-1257V, 2021 WL 1851491 (Fed. Cl. Spec. Mstr. Apr. 2, 2021) (finding that the flu vaccine caused petitioner's optic neuritis).

Moreover, molecular mimicry has also been accepted as a sound and reliable theory in other Prevnar13-GBS cases. *See e.g.*, *Gross v. Sec'y of Health & Hum. Servs.*, No. 17-1075V, 2022 WL 9669651, at *36 (Fed. Cl. Spec. Mstr. Sept. 22, 2022) (holding that the scientific support offered by petitioner's expert, including identification of components of the Prevnar vaccine that could create cross-reactive antibodies and reputable medical studies to support a phosphoglycerol theory satisfied *Althen* prong one); *Koller v. Sec'y of Health & Hum. Servs.*, No. 16-439V, 2021 WL 5027947, at *20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021) (finding that the identification of homologies "between a non-sugar component of the pneumococcal vaccine and components in the myelin," as supported by medical articles was sufficient to support molecular mimicry as the causal theory). Notably, mimicry between the phosphoglycerol sidechains, which are a necessary component of the vaccine, and the phosphate polar headgroup in the myelin has been demonstrated and found to be a sound and reliable theory in *Koller, Pierson, Gross, Maloney, Sprenger, Anderson* and others. Mimicry between protein components in the CRM197 conjugate and Contactin1 in the myelin of the peripheral nerves, as proposed by Dr. Axelrod in the present case, has also been found to be sound and reliable in other Prevnar 13-GBS cases. *See Maloney v. Sec'y of Health & Hum. Servs.*, No. 19-1713V, 2022 WL 1074087, at *32 (Fed. Cl. Spec. Mstr. Mar. 17, 2022) (finding that "there is also evidence to support Dr. Steinman's second theory based on CRM197 and Contactin1."); *Gross*, 2022 WL 9669651, at *36 (Fed. Cl. Spec. Mstr. Sept. 22, 2022) (findings that Dr. Steinman's identification of "sequences of shared homology between the proteins in the vaccine and those in Contactin1" was evidence supporting his theory of molecular mimicry between the two); *see also Sprenger v. Sec'y of Health & Hum. Servs.*, No. 18-279V, 2023 WL 8543435, at *19 (Fed. Cl. Spec. Mstr. Nov. 14, 2023). Many of the above cited cases propose both theories. *See, e.g.*, *Maloney*, 2022

WL 9669651, at *31; *see also Anderson v. Sec'y of Health & Hum. Servs.*, No. 18-484V, 2024 WL 557052, at *31-32 (Fed. Cl. Spec. Mstr. Jan. 17, 2024).[34]

In a recent opinion with a remarkably similar set of facts to the present case, Special Master Dorsey found entitlement based in significant part on the theory of mimicry between CRM197 and Contactin1. *Anderson*, 2024 WL 557052; Pet'r Ex. 70. In that case, the deceased developed severe abdominal pain beginning about a week after receiving the Prevnar vaccine. Dr. Kelkar opined that the deceased "developed rapidly evolving quadriparesis and areflexia leading to respiratory failure within a few days following [Prevnar 13] vaccination." *Anderson*, 2024 WL 557052, at *20. The clinical course, laboratory tests, and electrophysiologic tests in *Anderson* confirmed a diagnosis of axonal GBS. *Id.* at *6. Mr. Meyer did not respond to IVIG or plasmapheresis and succumbed to pulmonary complications. *Id.* at 5. Mr. Meyer had no other confounding factors such as infections at the onset of GBS. *Id.* at 4-5. Therefore, Dr. Kelkar concluded that "more likely than not, to a reasonable degree of medical certainty, the [Prevnar 13] vaccine served as a trigger for this process." *Id.* at *7.

In the present case, petitioner's symptoms evolved in a similar manner beginning with non-specific pain in the feet and ankles about four days after vaccination, evolving to increasing pain, weakness and areflexia and then rapidly to quadriparesis and respiratory insufficiency requiring intubation over the next several days. While petitioner did not succumb to the disease as in *Anderson*, she has remained severely impaired to the present time.

While I am not bound by the opinions of other special masters or of myself in other cases I do find the logic of these decisions to be persuasive. The theory proposed in most of those cases is the same as that proposed by Drs. Axelrod and Andersson in this case. As definitive scientific proof of this mechanism is beyond the current state of scientific knowledge, it would be impossible for a petitioner to satisfy the criteria endorsed by Dr. Whitton. The fulfillment of the criteria requiring *strong* or *robust* proof of specific biological mechanisms when such does not exist in the body of current scientific knowledge would be a bar too high and inconsistent with the purpose and nature of the vaccine compensation program. *See Sprenger*, 2023 WL 8543435, at *18.

The petitioner is required to show a sound and reliable theory explaining how the vaccine could have caused the injury to the petitioner. *Knudsen*, 35 F.3d at 548. The petitioner's theory is not required to be scientifically or medically certain but must be informed by a "sound and reliable" medical explanation. *Andreu*, 569 F.3d at 1380; *Boatmon*, 941 F.3d at 1359. I conclude that the explanation of petitioner's causation theories by Drs. Andersson and Axelrod are sound

[34] The undersigned recognizes that there is not uniformity between the special masters in decisions addressing the Prevnar 13 vaccine and GBS. *See, e.g.*, *Deshler v. Sec'y of Health & Hum. Servs.*, No. 16-1070V, 2020 WL 4593162, at *19 (Fed. Cl. Spec. Mstr. July 1, 2020); *Trollinger v. Sec'y of Health & Hum. Servs.*, No. 16-473V, 2023 WL 2521912, at *26 (Fed. Cl. Spec. Mstr. Feb. 17, 2023), mot. for review denied, 167 Fed. Cl. 127; *Bielak v. Sec'y of Health & Hum. Servs.*, No. 18-761V, 2023 WL 35509, at *31-32 (Fed. Cl. Spec. Mstr. Jan. 3, 2023); *Gamboa-Avila v. Sec'y of Health & Hum. Servs.*, No. 18-925V, 2023 WL 6536207, at *25 (Fed. Cl. Spec. Mstr. Sept. 11, 2023); *McConnell v. Sec'y of Health & Hum. Servs.*, No. 18-1051V, 2022 WL 4008238, at *9 (Fed. Cl. Spec. Mstr. Aug. 19, 2022). The undersigned acknowledges these cases but also notes that the decisions of other special masters or Court of Federal Claims' judges are not binding on special masters. *Boatmon*, 941 F.3d at 1358; Hanlon, 40 Fed. Cl. at 630.

and reliable. The experts provided numerous medical articles supporting such theory. I find persuasive the explanation that causation is multi-factorial and is most often triggered by an exogenous antigen. I find it likely that an exogenous antigen, in this case, the CRM197 conjugate in the Prevnar vaccine, which Dr. Axelrod demonstrated shared various similar peptides with key components of the peripheral nerves, began a cross reactive process. The immune response likely delivered the desired response to the vaccine itself but also recognized similar peptides in proteins in the peripheral nerves. Additionally, the potential of T cell degeneracy, the stimulation of complement and macrophages and failure of the T regulatory system in controlling the immune response to the vaccine, or some combination of these likely became the multi-factorial process, theorized by Dr. Axelrod. Dr. Whitton also agreed that the process of developing an autoimmune disease is probably multi-factorial and that molecular mimicry can be one step in that process. Tr. 339. While he proffered multiple possible mechanisms for autoimmune disease, he did agree that some autoimmune diseases are triggered by exogenous antigens, and the combination of susceptibility, whether genetic or otherwise, a failure of tolerance and or failure of the regulatory system can combine to result in an autoimmune disease such as GBS. Tr. 344-45. Dr. Donofrio agreed that molecular mimicry is accepted in the medical community as one potential cause of GBS. Tr. 274. He testified that the mimicry would have to be with antigens in the peripheral nerves. This, of course, is the mechanism proposed in petitioner's expert's theories.

Thus, after consideration of the evidence presented in this case, I conclude that the petitioner has demonstrated by preponderant evidence a sound and reliable medical theory to explain how the Prevnar 13 vaccine can cause GBS. As such, petitioner has satisfied *Althen* prong one.

b. *Althen* Prong Two

To satisfy *Althen* Prong two, petitioner must show by a preponderance of the evidence that there was a "logical sequence of cause and effect showing that the vaccine was the reason for the injury." *Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278.) "Petitioner must show that the vaccine was the but for cause of the harm…or in other words, that the vaccine was the 'reason for the injury.'" *Pafford*, 451 F.3d at 1356. In evaluating whether this prong is satisfied, the opinion and views of treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326. Medical records and medical testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether there is a logical cause and effect. *Althen*, 418 F.3d at 1280; *see also Capizzano*, 440 F.3d at 1326. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the medical community to establish a logical cause and effect." *Id.* at 1325. Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. *Id.*

As I have concluded that the petitioner has satisfied *Althen* prong one, the analysis next turns to whether, through molecular mimicry, the Prevnar 13 vaccine petitioner received caused her GBS. Prong two looks to the appropriateness of the diagnosis, the course of the illness, and the logic of the explanation building upon the finding of immune cross reaction in Prong one. In this case, the experts for both parties agreed that petitioner was appropriately diagnosed with

GBS and that her symptoms began about four days after her vaccination on February 6, 2019. They also agreed that the vaccine is an immune stimulant, and that there were no other known immune stimulants affecting the petitioner in the weeks before the onset of her condition.

After receiving the Prevnar 13 vaccine on February 6, petitioner's symptoms began with non-specific pain in her ankles on February 10th for which she went to the emergency department but was sent home with a diagnosis of anxiety. Beginning on February 13, her pain became worse. On the evening of the 15th, she began to develop weakness in the lower extremities. She fell multiple times by the following day when her neighbors called an ambulance to transport her to Lovelace Medical Center. She was admitted to the hospital on February 16th, by which time her bilateral leg pain had progressed to significant weakness and numbness. Her condition deteriorated very rapidly over the next several days as she developed extreme weakness in all extremities, blurred vision, urinary incontinence, and respiratory insufficiency such that she was transferred to the ICU and intubated. She also experienced facial symptoms including weakness and ptosis. She received five days of IVIG which was completed by February 25, when she appeared somewhat better. However, her condition then continued to rapidly worsen such that, by February 26, it was noted that her exam was "definitely worse" than the day before and she was documented to have 2/5 weakness in all extremities, inability to walk, and areflexia in all limbs. She was unable to clench the examiner's fingers and required further intubation due to respiratory distress and hypoxia. On March 17, 2019 the petitioner was discharged to Covenant Health, a long-term care facility. As described in the testimony, she subsequently resided in four long-term care or rehab facilities and has now moved to her daughter's home where she essentially requires full time care. Her condition began with ascending pain, numbness and weakness beginning in the distal lower extremities and progressed rapidly over about two weeks to the point of paralysis in all four limbs. Her condition essentially plateaued and has become permanent. She and her daughter explained that she is now able to hold her phone and type with one finger on it. She can hold a cup, but she cannot walk and requires assistance with all functions including bathing and toileting.

While no physician expressly opined in the medical records that the Prevnar vaccine was the cause of petitioner's GBS, it appeared to be considered as a cause, at least in the absence of an alternative explanation. There were multiple references in the medical records to the fact that petitioner received the Prevnar vaccine days before the onset of her GBS. Dr. Asir Farooq, a board-certified internist with a hospital-based practice at Texas Tech University Health Science Center, treated petitioner beginning in December 2022 in the rehab hospital. He testified at trial that, when he assumed her care, he took a detailed history and that he understood that prior to February 19, she was in good health and was very functional and independent with no neurological deficits. Tr. 163. He understood that every other cause was ruled out and that it was thought that the vaccine could have contributed to her GBS. He said that they did aggressive therapy in the rehab facility, but she did not improve significantly. Dr. Farooq did not treat petitioner at the onset of her disease, but, based on his experience in managing complex disability cases, the history he took, the clear diagnosis of GBS, and his treatment of her, he opined that it was likely that the Prevnar vaccine caused her GBS. *Id.* This testimony is entitled to some weight as coming from a physician with experience managing similarly complex cases, who treated petitioner during the course of this prolonged and devastating illness. Dr. Farooq's opinion accurately reflected the course of petitioner's illness, including her good health prior to

vaccination, the consideration of Prevnar as a cause by earlier treating physicians, and the fact that no other immune stimulus was identified.

In addition to providing medical records and testimony from one of her treating physicians, petitioner's experts provided support for *Athen* Prong two. Drs. Andersson and Axelrod opined that the Prevnar 13 vaccine petitioner received most likely caused her GBS. Dr. Andersson explained the process by which GBS progresses after being triggered by the immune response to the vaccine. Dr. Andersson explained that once the B cells are stimulated by the foreign invader, in this case the vaccine, they mature into plasma cells which produce up to 2,000 antibodies per second which circulate through the body opsonizing cells with similar structures for destruction by complement and macrophages. He testified that to the extent that there are similar epitopes present on host peripheral nerves, the vaccine can trigger the immune cells in the host through the effector mechanisms to produce injury to the peripheral nerves. Tr. 108. Dr. Andersson testified that petitioner's course was consistent with this theory and with the clinical way in which a severe case of GBS would be expected to present. *Id.* at 107-09, 112-14. As a practicing neurologist, Dr. Andersson opined that upon his review of this case that he had concluded that Ms. Byrd had post vaccination Guillain Barre' syndrome. He explained that as occurred in this case, GBS commonly presents with non-specific pain symptoms which are often not recognized as part of GBS on the initial exam. Subsequently, subtle signs like diminished reflexes and a predominantly ascending syndrome starting in the legs occurs, then it can go up to the chest and arms and sometimes the cranial nerves. He said that when you have an attack on the nerves it is usually the longest nerves that are affected first thus explaining why the symptoms usually begin in the lower legs or feet. You lose reflexes. He said that the cranial and autonomic nerves can become involved which affects your breathing and your heart. He said GBS is a monophasic disease. *Id.* at 108-110. After, the initiation of the immune response, Ms. Byrd's symptoms developed in a monophasic manner, over a period of several weeks initially with pain in her feet and ankles and then ascending through her legs and going up to the chest, upper extremities and affecting the autonomic nerves as well, consistent with the general GBS course he described.

Dr. Axelrod, in his expert report, pointed to a 2021 article by Querol and Lleixa as mentioned above. Those authors noted that a subset of GBS patients associated with antibodies against nodal and paranodal proteins including neurofascin, Contactin1, and CASPR1. They stated that most of these patients have aggressive presentations of autoimmune nodopathies that respond poorly to conventional GBS therapies. Ex 34 at 8. This presentation closely described the clinical presentation of Ms. Byrd who suffered a very aggressive form of GBS that responded poorly to treatment.

Respondent's expert, Dr. Whitton, testified that "if Prevnar 13 were to trigger GBS" through molecular mimicry, "it is more likely to be via CRM 197 than the other polysaccharides." *Id.* at 402. Dr. Whitton also testified that "some forms of GBS are clearly autoimmune and particularly need to involve molecular mimicry," including AMAN and AMSAN, the axonal form with which petitioner was diagnosed. *See id.* at 309.

Again, in this case, there was no dispute as to the receipt of the vaccine, the time to onset of the disease, the diagnosis of a severe form of GBS, or the fact that there was no other known immune stimulant which could have caused petitioner's GBS. Prior to the vaccination, petitioner

was healthy and functional, as illustrated by the fact that she was swimming a mile at a time three times per week prior to the onset of her GBS. GBS is recognized to be an ascending paralysis, usually beginning with symptoms in the distal extremities, as was the case with petitioner. The disease generally progresses rapidly within days and either begins to get better or plateaus within four to six weeks. Ms. Byrd's illness rapidly progressed particularly from February 15 forward and plateaued between the end of the month and the middle of March, but caused long-term paralysis which is now permanent. Dr. Donofrio agreed that someone who contracts severe GBS, as petitioner did, can go on to have very significant, permanent disability. Tr. 281-82.

I find that petitioner has provided preponderant evidence of a logical sequence of cause and effect between the Prevnar 13 vaccine and Ms. Byrd's GBS via molecular mimicry based on the expert opinion, petitioner's clinical course, the opinion of petitioner's treating provider, and the lack of evidence to support an alternative cause as described above. The process leading to her GBS was most likely initiated by the immune stimulus of the Prevnar vaccine and the cross-reactive response of her immune system to the vaccine and components of the peripheral nerves most likely in the nodal and paranodal areas. I conclude that petitioner has demonstrated, by preponderant evidence, a logical cause and effect in that, once the cross reaction was initiated by molecular mimicry between CRM197 and the nodal and paranodal proteins, it progressed rapidly and aggressively to a severe form of the disease. She was likely susceptible to such cross reaction and the failure tolerance and of her regulatory system to control the response likely allowed the progression in the manner that it did. The onset and aggressive progression of the axonal form of the disease, which responded poorly to treatment, occurred consistently with the cases described by Querol and Lleixa and occurred in a reasonable period of time with no alternative explanation. As such, petitioner has satisfied *Althen* prong two.

c. *Althen* prong three

Althen prong three requires that petitioner must establish the "timeframe for which it is medically acceptable to infer causation," and that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542-43 (2011)*, recons. denied after remand on other grounds,* 105 Fed. Cl. 353 (2012), *aff'd without op*., 503 F.App'x 952 (Fed. Cir. 2013).

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d. at 1278. The special master cannot infer causation from temporal proximity alone. *Thibaudeau v. Sec'y of Health & Human Servs.*, 24 Cl. Ct. 400, 403-04 (1991); *see also Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144 (Fed. Cir. 1992) ("[T]he inoculation is not the cause of every event that occurs within the ten-day period…[w]ithout more, this proximate temporal relationship will not support a finding of causation.")(quoting *Hasler v. U.S.*, 718 F.2d 202, 205 (6th Cir. 1983)).

Petitioner began to experience symptoms in her feet and ankles about four days after she received the Prevnar vaccine, as evidenced by her medical records. These initial symptoms did not result in a definitive diagnosis, but that diagnosis became clear over the following days to

weeks as she developed ascending paralysis that ultimately impaired her almost entirely. Dr. Andersson testified that an acceptable window of time from vaccine to onset of illness is fairly wide at about two to thirty-four days. Considering onset of four days when her initial ankle and foot pain occurred to seven days when the disease process began to become more severe, he opined that the timing was appropriate for an active immune response to the vaccine.

Dr. Axelrod also noted that Ms. Byrd had received the TDaP vaccine in 2016 which contains the diphtheria toxin that is the basis of CRM197 and also had received the pneumococcal 23 vaccine before which contains twelve of the thirteen antigens in Prevnar. Tr. 181. He opined that because she had the prior vaccines containing the same or similar antigens that it would be likely that she could have had a secondary or more rapid response of the adaptive immune system to the Prevnar because her system had been primed by the other vaccines. He opined that four days was appropriate timing for the onset of her GBS. Tr. 210.

Dr. Donofrio declined to opine on timing as he did not think there was a causal relationship to the vaccination, but he testified that he was not saying the timing was inappropriate either. Tr. 282. Dr. Whitton recognized that the Vaccine Program has generally accepted a window of three to forty-two days as acceptable timing for onset of an autoimmune condition after vaccination. He tended to think three days was too fast, but because at four days her onset was clearly within that window he does not dispute the timing either. *Id.*at 404.

Based on the testimony of the experts and petitioner's clinical course, I find that petitioner has provided preponderant evidence of a medically appropriate timeframe and that the onset of her condition occurred within such timeframe. Thus, petitioner has satisfied *Althen* prong three.

V. CONCLUSION

As I have found that the petitioner has provided preponderant evidence to satisfy all three *Althen* prongs, she is entitled to compensation. I will further note that the medical records and testimony provided at the hearing in this case have provided virtually undisputable evidence that the severity and permanence of petitioner's Guillain Barre syndrome easily justifies an award of the statutory cap of $250,000 for past pain and suffering. Given the severity of the injury, the degree of impairment, and the devastating impact that it has had on petitioner's finances as well as those of her daughter, I direct the parties to promptly begin to develop the proof of out of pocket expenses and life care plans in order to help to stabilize her finances which have been severely impacted by her GBS and to provide her with whatever rehabilitation care, equipment, and therapy may help to improve her quality of life and/or improve her function. A damages order will follow.

IT IS SO ORDERED

s/ Thomas L. Gowen
Thomas L. Gowen
Special Master